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Cost-effectiveness of therapist-guided Internet-delivered Cognitive Behavior Therapy for pediatric Obsessive-Compulsive Disorder: Results from a Randomized Controlled Trial

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ABSTRACT

Objectives To evaluate the cost-effectiveness of a therapist-guided Internet-delivered cognitive behavior therapy (ICBT) intervention for adolescents with obsessive-compulsive disorder (OCD), compared to untreated patients on a waitlist.

Design Single-blinded randomized controlled trial.

Setting A research clinic within the regular child and adolescent mental health service in Stockholm, Sweden.

Participants Sixty-seven adolescents (12–17yrs) with a DSM-5 diagnosis of OCD.

Interventions Either a 12-week, therapist-guided ICBT intervention or a wait list condition of equal duration.

Primary outcome measures Cost data were collected at baseline and after treatment, including healthcare use, supportive resources, prescription drugs, prescription-free drugs, school absence and productivity loss, as well as the cost of ICBT. Health outcomes were defined as treatment responder rate and Quality Adjusted Life Years (QALYs) gain. Bootstrapped mixed model analyses were conducted comparing incremental costs and health outcomes between the groups, from the societal and healthcare perspectives.

Results Compared to waitlist control, ICBT generated substantial societal cost savings averaging -144.98USD (95% *CI* [-159.79, -130.16]) per patient. The cost reductions were mainly driven by reduced healthcare use in the ICBT group. From the societal perspective, the probability of ICBT being cost-saving compared to waitlist control was approximately 60%. From the healthcare perspective, the cost

per additional responder to ICBT compared to waitlist control was approximately 2.29 USD.

Conclusions The results suggest that therapist-guided ICBT is a cost-effective treatment and results in societal cost savings, compared to leaving patients untreated. Since, at present, most patients with OCD do not have access to evidence-based treatments, the results have important implications for the increasingly strained national and healthcare budgets. Future studies should compare the cost-effectiveness of ICBT with regular face-to-face CBT.

Trial registration www.clinicaltrials.gov (NCT02191631)

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Study strengths include a randomized controlled trial design and blinded assessors of the clinical outcome as well as robust statistical methods (mixed models in combination with bootstrapped sampling).
- In addition, cost analyses were conducted from a societal and healthcare perspective, including a wide range of cost variables.
- The study results are limited by a moderate sample size and measurements at two time points (before and after intervention).
- Bigger sample sizes, more frequent measurements and longer, controlled follow-up time points should be implemented in future replications to allow for broader generalizability.

INTRODUCTION

Obsessive-Compulsive disorder (OCD) is characterized by anxiety-provoking intrusive thoughts or urges (obsessions), coupled in most cases with excessive and ritualistic behaviors (compulsions) [1]. OCD has a prevalence between 0.25 to 2 % in the child and adolescent population [2,3] and is associated with substantial reductions in health-related quality of life [4,5], as well as impairments in education, social relations, and family functioning [6]. The societal cost of OCD in adults in the USA is estimated to 10.6 billion USD per year [7].

International guidelines, such as those published by the American Academy of Child and Adolescent Psychiatry [8] and NICE [9] recommend cognitive behavioral therapy (CBT) as the first line treatment for young people with OCD. CBT is effective for the majority of patients, with effect sizes averaging g=1.2 [10]. However, a majority of patients do not have access to high quality CBT [11], due to a range of reasons, including shortage of therapists, geographical barriers, limited availability of specialized care and patients' delayed help seeking [12,13]. To overcome these challenges, internet-delivered CBT (ICBT) has emerged as a treatment format that is not bound to temporal or geographic barriers [14]. In ICBT, the patient works with the same content and homework tasks as in traditional face-to-face CBT (for example, psychoeducation, exposure and response prevention, relapse prevention), the only difference being that the treatment is delivered entirely via the Internet. ICBT is most effective when patients receive support from a clinician [15,16]. Typically, the clinician communicates with the patients via asynchronous online messages, thus not requiring booked appointments.

In adults, ICBT has been evaluated in over 100 randomized controlled trials (RCTs) for a range of different psychiatric conditions and results have shown effect sizes that were in the same range as those of face-to-face CBT [17]. The development of ICBT for the pediatric population however, has been lagging behind considerably, with currently only 19 randomized controlled trials in all psychiatric and somatic diagnostic domains [18]. Our research group has recently developed a therapist-guided ICBT protocol for pediatric OCD, which we initially evaluated in an open feasibility trial (*N*=21). Results showed significant and large improvements in OCD symptoms from pre- to post-treatment and high satisfaction with the treatment [19]. A subsequent RCT compared ICBT against a waitlist control in a group of 67 adolescents with OCD. Results showed that ICBT was highly acceptable and superior to a waitlist control [20]. Further, patients continued improving during the follow-up period. The average clinician support time was only 17.5 minutes per patient/week. Thus, ICBT has the potential to reduce treatment costs and being a cost-effective treatment due to its high degree of accessibility and reduced therapist contact.

Although ICBT has shown promise in terms of effectiveness in many mental health conditions, there have been few health economic evaluations. In a comprehensive review that included studies from the adult and child/adolescent ICBT field, only five of the 139 screened studies included a cost-effectiveness evaluation; three of those were excluded due to methodological issues, and none of the studies involved children/adolescents [21]. In adults with OCD, only three cost-effectiveness evaluations have been conducted for computerized or Internet-based CBT. In one study comparing entirely self-guided, computer-aided CBT with standard face-to-face CBT and relaxation, computer-aided CBT was less effective

than face-to-face CBT, but, given the lower therapist cost of this treatment, computer-aided CBT produced more benefit per unit cost [22]. In another study comparing therapist-guided ICBT with an online supportive therapy control condition [23], ICBT was a cost-effective treatment with an average cost of 931 USD for one additional treatment responder and 7186 USD per quality adjusted life year (QALY) gained. In a third study, Andersson et al. evaluated the cost-effectiveness of a post-treatment booster program in order to help patients maintain treatment gains after therapist-guided ICBT [24]. On average, the cost of one avoided relapse by providing booster ICBT vs. no additional treatment was estimated to be 1066-1489 USD. To our knowledge, there have been no previous studies evaluating the cost-effectiveness of ICBT for pediatric OCD.

This paper reports the cost-effectiveness of therapist-guided ICBT for adolescents with OCD, compared to a waitlist control condition, from both a societal as well as a healthcare perspective. We hypothesized that ICBT would result in a reduction in societal costs, originating from reduced health care utilization and increased of academic functioning, amongst other indicators.

METHODS

Study design

Cost-effectiveness data was collected in tandem with a randomized controlled trial [20]. Adolescents (*N*=67) with OCD were randomized to either ICBT (*n*=33) or a waitlist control (*n*=34), each of 12 weeks duration. Assessment points for the data collection were pre-treatment and post-treatment. The assessors of the primary

clinical outcome measure were blinded for group allocation. The trial design and study flow is presented in **Figure 1**. The study was approved by the Regional Ethical Review Board in Stockholm, Sweden (2014/673-31/2) and registered on clinicaltrials.gov (NCT02191631).

Study sample

Patients were eligible if they were 12 to 17 years of age, fulfilled criteria for OCD [1] and had moderate to severe symptom severity (i.e. at least 16 points on the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) [25], were able to communicate in Swedish, had access to the internet and a parent to co-participate in the intervention. Patients on psychotropic medication were required to be on a stable dose for the last 6 weeks prior to baseline assessment. Comorbidity was allowed except for conditions with a different treatment indication e.g. autism spectrum disorder, psychosis, bipolar disorder, severe eating disorder, suicidal ideation, substance abuse. Patients that had completed CBT for OCD 12 months prior to baseline assessment or had an ongoing CBT treatment were excluded from the study. Information on the study sample is presented in Table 1. There were no statistically significant baseline differences between the ICBT and waitlist group.

Table 1: Patients' characteristics

	Control (*n* = 34)		ICBT (*n* = 33)		Total (*N* = 67)	
Sex (% girls)	41%		52%		46%	
Age (M, SD)	14,97	(1,66)	14,21	(1,69)	14,60	(1,71)
Country of birth (%)						
Sweden	88%		97%		93%	
Other European	6%		3%		4%	
Asian	6%		0%		3%	
Parent's educational level (%)						
Primary	0%		3%		1%	
High school	29%		21%		25%	
College	3%		6%		4%	
Vocational	6%		3%		4%	
University	50%		48%		49%	
Doctoral degree	0%		3%		1%	
Other	12%		15%		13%	
OCD symptom severity baseline score, CY-BOCS (M, SD)	22,12	(3,91)	23,00	(4,31)	22,55	(4,10)
Number of comorbid diagnoses (%)						
0	53%		61%		57%	
1	35%		21%		28%	
2	9%		9%		9%	
3	3%		6%		4%	
4	0%		3%		1%	
Medication (on-going)						
None	82%		72%		78%	
SSRI	18%		18%		18%	
Stimulants	3%		6%		4%	
Tricyclic antidepressants	0%		3%		1%	
Type of referral						
Self-referral	91%		94%		93%	
CAMHS referral	9%		6%		7%	

Abbreviations: ICBT = internet-delivered cognitive behavior therapy; OCD = obsessive-compulsive disorder; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; SSRI = Selective serotonin reuptake inhibitor; CAMHS = Child and Adolescent Mental Health Service

Intervention

The ICBT intervention, “BiP OCD”, has been previously tested in an open feasibility trial [19,26] and recently in a 12-week waitlist-controlled RCT [20]. BiP OCD is a web-based, therapist-guided and parent-assisted CBT intervention with treatment components in line with clinical expert guidelines for OCD treatment, namely psychoeducation, exposure with response prevention, cognitive restructuring and relapse prevention [27]. The treatment content is age-tailored for 12 to 17 year olds with texts to read, short videos to watch and exercises to work with. The treatment content is presented in 12 chapters that are consecutively unlocked by the patient. A clinical psychologist provides asynchronous written feedback 5 days a week via messages through the secure Internet portal, and occasionally via telephone calls. Adolescents access their personal content via password and text-message secured login. Parents participate in the treatment through parent-specific chapters, with varying degrees of parental involvement depending on the child’s age. A more detailed description of BiP OCD can be found elsewhere [19,20,26].

During the 12-week study period, patients on the waitlist control were allowed to continue any medication and psychosocial care except those specified in the exclusion criteria for the study (ongoing CBT).

Economic evaluation

Health economics is the application of economics principles on health and healthcare [28]. Cost-effectiveness analysis is a branch of health economics concerned with the comparative analysis of the incremental differences in costs and

effects of alternative interventions for a given health condition. The result of the analysis is usually presented as an incremental cost-effectiveness ratio (ICER), where the difference in costs is divided by the difference in effects [29].

The economic evaluation framework of this study was a within trial cost-effectiveness analysis undertaken from a societal perspective (including costs associated with healthcare, education and individual patients) and, separately, a healthcare perspective (including only costs associated with healthcare).

The time horizon was 12 weeks, which mirrors the duration of the intervention. Costs were collected in tandem with our RCT in Swedish Krona (SEK) and presented in US dollars (USD) using the purchasing power parity (PPP) estimates [30].

Costs

Two categories of costs were estimated, costs for the ICBT intervention and other societal costs involving costs that arose on the side of the healthcare and educational system as well as costs that arose for patients directly.

Intervention costs included cost for the clinicians' time for the 12 weeks of ICBT as well as ICBT treatment platform maintenance costs. Clinician times (on average 17.5 minutes per patient/week) included writing messages to the patients and telephone calls and were multiplied by the average hourly psychologist wage in Stockholm County (**Online supplement 1**). Maintenance costs were associated with the technical platform that ICBT runs on, such as external IT support, technical upgrades and iterative development of platform functionality. Maintenance costs were estimated to be 4390.4 USD for 12 weeks of the intervention.

Other societal costs were collected using an adapted version of the parent-rated Trimbos Questionnaire for Costs associated with Psychiatric Illness (TiC-P) [31] at baseline and post-treatment. The questionnaire includes items on healthcare resource use (e.g. medical doctor or psychologist visits), supportive resources (e.g. private tutoring), medications, prescription-free drugs or supplements, absenteeism from school and academic productivity loss when being at school despite not feeling well. Information on parental productivity loss was also collected, but due to an error in the wording of the questionnaire, that information could not be used in the analyses. Costs were estimated by the product of unit costs and frequencies, e.g. costs for doctors' visits*number of visits. Thus, the overall societal cost pertaining to each intervention arm was the cumulative cost over the treatment period (12 weeks). As TiC-P covers a 4-week timeframe, the costs for the first and second month of the study period were estimated by linear interpolation using baseline and 12-week data. Unit costs as well as their sources are displayed in **Online supplement 1**.

Intervention costs and other societal costs were summed up to *total societal costs*. Further, intervention costs, costs for healthcare utilization and medications were summed up to *total healthcare costs*.

Health outcomes

The primary health outcome was defined as "treatment responder rate". In line with expert consensus [32], patients were classified as responders if they had shown a decrease of symptoms on the CY-BOCS of at least 35% at post-treatment and had a clinical global improvement rating (CGI-I) [33] of 1="very much improved" or 2="much improved".

The secondary health outcome was defined as gains in quality adjusted life years (QALYs). Patients filled in the European Quality of life Five Dimensions Questionnaire Youth version (EQ-5D-Y), to assess health-related quality of life [34]. EQ-5D is a widely used measure in health economic evaluations and consists of 5 dimensions measuring health-related functioning and quality of life i.e. pain/discomfort, anxiety/depression, self-care, mobility and usual activities. It also consists of a 0 - 100 visual analogue scale (VAS) used to measure subjective ratings of health. The EQ-5D-Y was chosen given the study sample age (12-17 years) and had previously shown feasibility of use in a Swedish pediatric population [35]. The health profiles derived from the EQ-5D-Y were used to estimate quality of life adjusted life years (QALYs), ranging from 0 to 1, with 1 representing one year of perfect health. The Swedish EQ-5D adult population value sets were used as a proxy in the calculation of QALYs [36], given that the adolescent value sets are not yet available. The change in QALYs was then corrected for the intervention period expressed in years (i.e. 3 months = 0.25 of a year).

Statistical analyses

The pre-treatment differences in costs were tested using non-parametric Mann-Whitney tests. Treatment effects on responder rates between ICBT and waitlist were analyzed using Fisher's exact test while incremental differences in QALYs and costs between the intervention and waitlist control groups over time were analyzed using mixed effects models. Mixed effects models are equipped to analyze longitudinal data and are effective in handling of missing data [37], thus were deemed fit for these analyses. Since the cost data were skewed (Shapiro-Wilk test of normality $z=7.05$, $p<.001$), mixed models analyses were carried out with 5000 non-parametric bootstrap samplings to create normally distributed mean values for further analyses.

Cost-effectiveness analyses

Two types of cost-effectiveness analyses were conducted: a cost-effectiveness analysis using responder rates as the primary health outcome and a cost-utility analysis using QALYs as a secondary health outcome. An incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in total costs by the difference in responder rate, as well as in QALYs, between the ICBT and waitlist groups.

The bootstrapped results, pairings of the differences in costs with the differences in health outcomes, were represented visually on a cost-effectiveness plane **(Online supplement 2 and 3)**. The cost-effectiveness plane depicts the uncertainty around the cost-effectiveness estimate, the ICER. The horizontal axis divides the plane according to incremental effect and the vertical axis according to incremental societal cost, which divides the plane into four different quadrants. Iterations plotted in the top right quadrant are those where the intervention is more effective and more costly than the comparator; those in the bottom right quadrant are more effective and less costly; those in the bottom left quadrant are less effective and less costly; and those in the top left quadrant are more costly and less effective [29]. To analyze the cost-effectiveness from a healthcare perspective, the ICER was estimated, comparing the differences in total healthcare costs and health outcomes between the ICBT group and waitlist control group. The probability of ICBT to be cost-effective was calculated, given different willingness-to-pay scenarios, presented visually by means of a cost-effectiveness acceptability curve (CEAC) produced using the net-benefit approach, i.e. $(\lambda \times E) - \Delta C$ where λ is the willingness to pay (i.e. the cost that the society is willing to pay for one unit of improvement), E is the health benefit and ΔC is the change in costs **(Figure 3)**.

The statistical significance was set at a p-value of 0.05 and 95% confidence intervals (*CI*). The calculations were done using STATA version 13 (StataCorp) and Excel 2013 (Microsoft).

Sensitivity analyses

A sensitivity analysis was carried out to test three scenarios that were thought to influence the final results. Firstly, we re-ran the cost-utility analysis using EQ-5D-Y VAS scores instead of the estimated EQ-5DY profile QALYs. This was because the QALYs used in the primary analysis were determined using an adult value set algorithm as the adolescent value-set was not yet available, thus a potential estimation error. Secondly, we calculated the correlations between EQ-5D-Y QALYs estimates, EQ-5D-Y VAS scores and the responder status in the study patients. This was to test whether the different outcome measures were strongly associated with each other, which would further strengthen the validity of the measures. Lastly, we repeated the cost-effectiveness analyses with the intervention costs increased by 50% in order to cater for changes in ICBT platform maintenance and clinician time costs, thus testing the robustness of the cost-effectiveness result given inflated costs.

RESULTS

Costs

The mean intervention cost per ICBT patient was estimated as maintenance costs of 65.98 USD and clinician's time of 121.39 USD, i.e. a total of 187.37 USD per patient (bootstrapped estimate of 196.66 USD).

There were no total societal cost differences between the two groups at baseline (z=-1.09, p=.28). After treatment, the average overall societal cost difference between ICBT and waitlist control was M=-144.98 USD (95% CI[- 159.79 , -130.16]) per patient, indicating cost savings of ICBT compared to waitlist. There was an increase of healthcare use (i.e. clinician visits) in the waitlist control compared to intervention group resulting into a M=-162.21 USD difference (95% CI[- 173.32 , -151.32]), which was the main driver of the overall cost difference. The average total healthcare cost difference was M=21 USD per patient, indicating additional costs of ICBT compared to waitlist.

For a complete presentation of baseline costs and cost changes over the 12-week intervention period, see **Table 2.** For differences in cost changes see **Figure 2**.

Table 2: Estimated baseline and pre- to post-intervention change scores for societal costs, intervention costs and health outcomes, per patient

		Baseline				Pre- to post-intervention					
		ICBT		Waitlist		ICBT		Waitlist		Cost-difference ICBT vs waitlist*	
		Mean	95% CI	Mean	95% CI	Mean change	95% CI	Mean change	95% CI	Mean difference	95% CI
ICBT intervention costs	Clinician time & platform maintenance	-	-	-	-	196.66	196.33-196.98	0	0	196.66	196.33-196.98
Other societal costs	Healthcare use	425.66	237.08-614.25	323.63	190.75-456.50	-71.21*	-79.86 - -62.58	90.99	84.42-97.57	-162.21*	-173.32 - -151.32
	Medicines	32.20	13.77-51.58	18.66	0 - 38.28	-28.88*	-29.74 - -28.01	-15.80*	-16.64 - -14.97	-13.07*	-14.27 - -11.88
Total health care costs		**457.86**	**261.30-654.42**	**342.29**	**208.78-475.79**	**96.57**	**87.56-105.56**	**75.19**	**68.56-81.82**	**20.57**	**9.78-31.36**
	Supportive resources	48.09	-0.97-98.11	16.24	-0.52-33.01	78.52	75.97-81.06	132.77	131.39-134.15	-54.25*	-57.13 - -51.37
	Prescription-free drugs & supplements	19.06	-11.72-50.80	8.97	1.41-16.50	-32.47*	-33.83 - -31.11	-6.62*	-6.96 - -6.28	-25.85*	-27.26 - -24.45
	School absence	129.47	25.34-233.60	70.02	36.29-103.77	56.82	52.09-61.55	101.25	99.02-103.48	-44.43*	-49.65 - -39.06
	Academic production loss	43.87	8.46-79.28	32.74	-4.88-70.37	83.04	80.83-85.25	125.13	123.01-127.25	-42.09*	-45.12 - -39.21
Total societal costs		**698.36**	**421.51-975.21**	**470.26**	**317.41-623.11**	**282.74**	**270.30-295.17**	**427.72**	**419.57-435.86**	**-144.98***	**-159.79 - -130.16**

Health outcomes	Number of Treatment responders (%)	-	-	-	-	27%	20-35%	0%	0%	27%	20-35%
	QALYs	.95	.95 - .96	.96	.95 - .97	-.0015#	-.005- -.0025	-.00075	-.005- - .0025	-.00065	-.00073 - -.00056
	VAS	66.11	58.60 - 73.61	66.20	58.80 - 73.59	.0007#	-.0168- .0181	-.0034	-.0169 - .0104	.0041	.0034-.0049

Note: # = Values have been multiplied with the adjustment factor of the intervention period of 3 months/one year i.e. 0.25; * = negative values indicating cost-savings of ICBT compared to waitlist. *Abbreviations:* ICBT=Internet-delivered Cognitive Behavior Therapy, CI=Confidence interval

Health outcomes

At post-intervention, there were nine (27%) strictly defined treatment responders in the ICBT group and none in the waitlist (Fisher's exact test, *p*=.001). There were no significant time*group effects in EQ-5D-Y estimated QALYs (*B*=.000, *z*=.01, *p*=.99) or in the EQ-5D-Y VAS scores (*B*=1.69, *z*=0.38, *p*=.71).

Cost-effectiveness analyses

The distribution of total societal cost differences and differences in treatment response of the bootstrapped estimations were centered in the south-east quadrant of the cost-effectiveness plane, indicating dominance of ICBT over waitlist (less costly and more effective), see **Online supplement 2**. Accordingly, the probability of ICBT to be cost saving was 59.4 percent. The distribution of cost differences and differences of QALYs were centered south of the midline at the origin, indicating less costs of ICBT but equal effect compared to waitlist, see **Online supplement 3**.

When analyzing cost effectiveness from a healthcare perspective, (i.e. Healthcare costs = cost of ICBT + medicines + healthcare use), the incremental cost effectiveness ratio (ICER) was estimated to 2.29 USD per responder. Considering a range of willingness-to-pay scenarios, the probability of ICBT to be cost-effective approximated 100% at 200 USD per responder (see cost-effectiveness acceptability curve in **Figure 3**).

Sensitivity analyses

Using the VAS scores instead of EQ-5D-Y estimated QALYs showed a minimal, non-significant increase of the ICBT group compared to the waitlist at the post-intervention assessment (**Table 2**) with *B*=1.69, *z*=0.38, *p*=.71.

The correlation between responder status and EQ-5D-Y estimated QALYs was examined, but found to be very low and non-significant (*r*=.16, *p*=.23). The correlation between responder status and VAS ratings was in the same range and non-significant (*r*=.18, *p*=.16). The correlation of EQ-5D-Y estimated QALYs and EQ-5D-Y VAS ratings was significant and in the small to moderate range (*r*=.27, *p*=.04).

When repeating the analysis with intervention costs raised by 50% to account for a scenario with increased maintenance and clinician expenses, the total cost difference was reduced to *M*=- 46.92 USD (95% *CI*[- 61.74, - 32.11]) per patient, however, ICBT was still cost saving compared to waitlist control.

DISCUSSION

To our knowledge, this is the first study to evaluate the cost-effectiveness of therapist-guided ICBT for pediatric OCD and one of the very few in the field of child and adolescent ICBT. The results indicated that ICBT is not only clinically superior but also results in cost savings, compared to leaving OCD patients untreated. ICBT resulted in societal cost savings of about 145 USD per patient and had an incremental response rate of 27%. The cost saving effects of ICBT were still observed when conservatively increasing the intervention cost by 50%. The main driver of the cost savings was a marked reduction in healthcare utilization in the ICBT group, with a mean cost saving of 162 USD in the ICBT group compared to the waitlist control. From a healthcare perspective, ICBT was cost effective compared to

the waitlist control with an average additional cost of 2.29 USD/responder. The probability of the intervention being cost effective plateaued at 100% when the willingness to pay was greater than 200 USD/percentage responder.

In light of the current cost developments, it is evident that mental healthcare increasingly strains national budgets. In the US over 300 billion dollars per year are spent on mental health considering disability benefits, healthcare costs and lost earnings [38]. Sweden, where the study was conducted, is no exception; 10.5 billion USD are spent per year on mental health disorders [39,40]. Consequently, efficient use of limited resources has become an important step in the evaluation of new treatments. In this context, this study makes an important contribution to the field in general and to the field of pediatric OCD in particular. The finding that therapist-guided ICBT is a cost-effective treatment and results in societal cost savings, compared to leaving patients untreated, suggests that integrating ICBT within the regular armamentarium of specialist OCD clinics or even regular child and adolescent psychiatry units, is likely to be a worthwhile investment for society.

Unexpectedly, ICBT did not yield any effects on QALYs. Sensitivity analyses revealed that both measures of QALYs (EQ-5D-Y health profiles and EQ-5D-Y VAS scores) were not correlated with the clinical outcome, and only weakly correlated with one another. This raises the question of whether the EQ-5D-Y is a suitable quality of life measure for our patient group. Previous studies were able to demonstrate a clear association of OCD symptoms with decreased quality of life,[4] as well as changes in quality of life following treatment for OCD.[5] However, those studies did not use the EQ-5D-Y. Because the scale's individual items are more focused on somatic aspects of quality of life, such as mobility and pain, it might not

accurately represent quality of life gains that are associated with reduced OCD symptoms. Notably, the utility values pre-intervention were already in the high range of the scale i.e. 0.95, and thus it is likely that a ceiling effect occurred. Furthermore, in absence of available norms for Swedish adolescents, we applied an adult algorithm in order to calculate QALYs. Consequently, future evaluations in this field should choose quality of life measures that are validated, appropriate for the patient population and sensitive to change.

Our results need to be interpreted in light of some study limitations. Firstly, the study is based on a modestly sized sample and, as the cost-effectiveness planes show, there is some uncertainty about the precision of the estimates. The results should therefore to be seen as preliminary and need replication in a larger sample. However, the societal cost difference 95% confidence interval did not cross zero (-159.79 to -130.16 USD), indicating that ICBT is indeed associated with substantial cost savings. Secondly, the societal costs were collected at baseline and post-treatment and were interpolated for time period in between, on the assumption that they varied linearly over time. OCD symptoms often decline linearly during treatment (e.g. Andersson et al. 2012), and therefore a linear cost development is a reasonable assumption, but as there is no empirical cost data for the time points between baseline and post-intervention this remains a factor of uncertainty. Future evaluations should employ more frequent cost measurements, covering the whole treatment and follow-up period. Thirdly, the study period covered only the short-term outcomes from the 12-week intervention phase. As the benefits of ICBT continue beyond the acute phase of the treatment and into the follow-up [19,20], a longer evaluation time frame would be appropriate and may possibly result in additional cost savings. Future studies should therefore extend the time frame to at least 3

months after treatment. A final limitation is the choice of control group. As most OCD patients do not receive CBT, the waiting-list comparator could still be regarded as an ecologically valid control condition. However, further evaluations should include comparisons with the gold standard treatment of pediatric OCD, face-to-face CBT. As the current study shows somewhat lower response rates than those found in face-to-face treatment [10], it is conceivable that ICBT may be less effective than face-to-face CBT, but still result in substantial cost savings.

To summarize, the results of this study show that therapist-guided ICBT is cost-effective compared to no treatment. Given the limitations of the current study, the results should be replicated in larger samples, employing more adequate measures of health-related quality of life, optimized cost measurements and longer follow-up periods to better capture both costs and health outcomes over time. Furthermore, a direct head-to-head comparison of therapist-guided ICBT with standard face-to-face CBT would be informative, as ICBT is hypothesized to generate cost savings compared to face-to-face CBT, even if ICBT were found to be less efficacious. Non-inferiority and stepped-care designs, combined with robust health economic evaluations should provide useful information for the design and optimization of specialist OCD clinics and child and adolescent psychiatry services in general.

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COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: all authors had financial support from Stockholm County Council, Swedish Research Council for Health, Working Life and Welfare and Jane & Dan Olsson Foundation for the submitted work; CR was supported by a grant from the Swedish Research Council; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

REFERENCES

1 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, DSM 5*. 5th ed. Arlington, VA: : American Psychiatric Publishing 2013.

2 Heyman I, Fombonne E, Simmons H, *et al.* Prevalence of obsessive-compulsive disorder in the British nationwide survey of child mental health. *Int Rev Psychiatry* 2003;**15**:178–84. doi:10.1080/0954026021000046146

3 Valleni-Basile LA, Garrison CZ, Jackson KL, *et al.* Frequency of obsessive-compulsive disorder in a community sample of young adolescents. *J Am Acad Child Adolesc Psychiatry* 1994;**33**:782–91. doi:10.1097/00004583-199407000-00002

4 Lack CW, Storch EA, Keeley ML, *et al.* Quality of life in children and adolescents with obsessive-compulsive disorder: base rates, parent–child agreement, and clinical correlates. *Soc Psychiatry Psychiatr Epidemiol* 2009;**44**:935–42. doi:10.1007/s00127-009-0013-9

5 Weidle B, Jozefiak T, Ivarsson T, *et al.* Quality of life in children with OCD with and without comorbidity. *Health Qual Life Outcomes* 2014;**12**:152. doi:10.1186/s12955-014-0152-x

6 Piacentini J, Bergman RL, Keller M, *et al.* Functional impairment in children and adolescents with obsessive-compulsive disorder. *J Child Adolesc Psychopharmacol* 2003;**13 Suppl 1**:S61-9. doi:10.1089/104454603322126359

7 Eaton WW, Martins SS, Nestadt G, *et al.* The burden of mental disorders. Epidemiol. Rev. 2008;**30**:1–14. doi:10.1093/epirev/mxn011

8 Geller DA, March J, AACAP Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2012;**51**:98–113. doi:10.1016/j.jaac.2011.09.019

9 NICE. Obsessive-compulsive disorder: Core interventions in the treatment of obsessive-compulsive disorder and body dysmorphic disorder. 2006.http://www.ncbi.nlm.nih.gov/books/NBK56458/ (accessed 18 Dec2012).

10 McGuire JF, Piacentini J, Lewin AB, *et al.* A Meta-Analysis of Cognitive Behavior Therapy and Medication for Child Obsessive-Compulsive Disorder: Moderators of Treatment Efficacy, Response, and Remission. *Depress Anxiety* 2015;**32**:580–93. doi:10.1002/da.22389

11 Goodwin R, Koenen KC, Hellman F, *et al.* Helpseeking and access to mental health treatment for obsessive-compulsive disorder. *Acta Psychiatr Scand* 2002;**106**:143–9. doi:10.1034/j.1600-0447.2002.01221.x

12 Simonds LM, Thorpe SJ. Attitudes toward obsessive-compulsive disorders--an experimental investigation. *Soc Psychiatry Psychiatr Epidemiol* 2003;**38**:331–6. doi:10.1007/s00127-003-0637-0

13 O'Neill J, Feusner JD. Cognitive-behavioral therapy for obsessive compulsive disorder: Access to treatment, prediction of long-term outcome with neuroimaging. Psychol. Res. Behav. Manag. 2015;**8**:211–23. doi:10.2147/PRBM.S75106

14 Andersson G. Using the Internet to provide cognitive behaviour therapy. *Behav Res Ther* 2009;**47**:175–80. doi:10.1016/j.brat.2009.01.010

15 Cuijpers P, Donker T, van Straten A, *et al.* Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies. *Psychol Med* 2010;**40**:1943–57. doi:10.1017/S0033291710000772

16 Cuijpers P, Donker T, Johansson R, *et al.* Self-guided psychological treatment for depressive symptoms: A meta-analysis. *PLoS One* 2011;**6**. doi:10.1371/journal.pone.0021274

17 Hedman E, Ljótsson B, Lindefors N. Cognitive behavior therapy via the Internet: a systematic review of applications, clinical efficacy and cost-effectiveness. *Expert Rev Pharmacoecon Outcomes Res* 2012;**12**:745–64. doi:10.1586/erp.12.67

18 Vigerland S, Lenhard F, Bonnert M, *et al.* Internet-delivered cognitive behavior therapy for children and adolescents: A systematic review and meta-analysis. *Clin Psychol Rev* 2016;**50**:1–10. doi:10.1016/j.cpr.2016.09.005

19 Lenhard F, Vigerland S, Andersson E, *et al.* Internet-delivered cognitive behavior therapy for adolescents with obsessive-compulsive disorder: An open trial. *PLoS One* 2014;**9**:e100773. doi:10.1371/journal.pone.0100773

20 Lenhard F, Andersson E, Mataix-Cols D, *et al.* Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Trial. *J Am Acad Child Adolesc Psychiatry* Published Online First: October 2016. doi:10.1016/j.jaac.2016.09.515

21 Arnberg FK, Linton SJ, Hultcrantz M, *et al.* Internet-delivered psychological treatments for mood and anxiety disorders: a systematic review of their efficacy, safety, and cost-effectiveness. *PLoS One* 2014;**9**:e98118. doi:10.1371/journal.pone.0098118

22 McCrone P, Marks IM, Greist JH, *et al.* Cost-effectiveness of computer-aided behaviour therapy for obsessive-compulsive disorder [1]. Psychother. Psychosom. 2007;**76**:249–50. doi:10.1159/000101504

23 Andersson E, Hedman E, Ljótsson B, *et al.* Cost-effectiveness of internet-

based cognitive behavior therapy for obsessive-compulsive disorder: Results from a randomized controlled trial. *J Obsessive Compuls Relat Disord* 2015;**4**:47–53. doi:10.1016/j.jocrd.2014.12.004

24 Andersson E, Ljótsson B, Hedman E, *et al.* Cost-effectiveness of an internet-based booster program for patients with obsessive–compulsive disorder: Results from a randomized controlled trial. *J Obsessive Compuls Relat Disord* 2015;**4**:14–9. doi:10.1016/j.jocrd.2014.10.002

25 Scahill L, Riddle MA, McSwiggin-Hardin M, *et al.* Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry* 1997;**36**:844–52. doi:10.1097/00004583-199706000-00023

26 Lenhard F, Vigerland S, Engberg H, *et al.* 'On My Own, but Not Alone' - Adolescents' Experiences of Internet-Delivered Cognitive Behavior Therapy for Obsessive-Compulsive Disorder. *PLoS One* 2016;**11**:e0164311. doi:10.1371/journal.pone.0164311

27 Franklin ME, Foa EB. Treatment of obsessive compulsive disorder. *Annu Rev Clin Psychol* 2011;**7**:229–43. doi:10.1146/annurev-clinpsy-032210-104533

28 Morris, Stephen A.; Devlin, Nancy; Parkin, David & Spencer A. *Economic Analysis in Healthcare*. 2nd ed. New Jersey: : Wiley 2012. https://books.google.se/books/about/Economic_Analysis_in_Healthcare.html?id=Co-JZwEACAAJ&pgis=1

29 Drummond MF, Sculpher MJ, Torrance GW, *et al. Methods for the economic evaluation of health care programmes*. 2005. http://econpapers.repec.org/RePEc:oxp:obooks:9780198529453

30 CCEMG, EPPI. CCEMG - EPPI-Centre Cost Converter. 2016.http://eppi.ioe.ac.uk/costconversion/default.aspx

31 Bouwmans C, De Jong K, Timman R, *et al.* Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). *BMC Health Serv Res* 2013;**13**:217. doi:10.1186/1472-6963-13-217

32 Hess NCL, Carlson DJ, Inder JD, *et al.* Clinically meaningful blood pressure reductions with low intensity isometric handgrip exercise. A randomized trial. *Physiol Res* 2016;**65**:461–8. doi:10.1017/CBO9781107415324.004

33 Guy W. *Assessment manual for psychopharmacology, revised*. Washington DC: : US Government Printing Office 1976.

34 Wille N, Badia X, Bonsel G, *et al.* Development of the EQ-5D-Y: A child-friendly version of the EQ-5D. *Qual Life Res* 2010;**19**:875–86. doi:10.1007/s11136-010-9648-y

35 Burström K, Bartonek Å, Broström EW, *et al.* EQ-5D-Y as a health-related quality of life measure in children and adolescents with functional disability in Sweden: testing feasibility and validity. *Acta Paediatr* 2014;**103**:426–35. doi:10.1111/apa.12557

36 Burström K, Sun S, Gerdtham UG, *et al.* Swedish experience-based value sets for EQ-5D health states. *Qual Life Res* 2014;**23**:431–42. doi:10.1007/s11136-013-0496-4

37 Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing

repeated-measures data and its reflection in papers published in the Archives of General Psychiatry. *Arch Gen Psychiatry* 2004;**61**:310–7. doi:10.1001/archpsyc.61.3.310

38 Kessler RC, Heeringa S, Lakoma MD, *et al.* Individual and societal effects of mental disorders on earnings in the United States: results from the national comorbidity survey replication. *Am J Psychiatry* 2008;**165**:703–11. doi:10.1176/appi.ajp.2008.08010126

39 OECD. *Mental Health and Work: Sweden*. OECD Publishing 2013. doi:10.1787/9789264188730-en

40 Tiainen A, Rehnberg C. The economic burden of psychiatric disorders in Sweden. *Int J Soc Psychiatry* 2010;**56**:515–26. doi:0020764009106140 [pii]\n10.1177/0020764009106140

41 Andersson E, Enander J, Andrén P, *et al.* Internet-based cognitive behaviour therapy for obsessive-compulsive disorder: a randomized controlled trial. *Psychol Med* 2012;**42**:2193–203. doi:10.1017/S0033291712000244

FIGURES & ONLINE SUPPLEMENTS

Figure 1: Study flow chart

Figure 2: Mean cost-changes from baseline to post-treatment for ICBT and waitlist (USD)

Figure 3: Cost-effectiveness acceptability curve

Online supplement 1: Unit costs and sources

Online supplement 2: Cost-effectiveness plane with bootstrapped differences in costs and responders (black represents mean estimate)

Online supplement 3: Cost-effectiveness plane with bootstrapped differences in costs and QALYs (black dot represents mean estimate)

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title page
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	p 4 - 6
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	p 8
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	p 10 - 12
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	p 10 - 12
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	p 9
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	p 6
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	n.a.
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	p 11- 12
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	p 6 - 7

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	n.a.
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n.a.
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	p 10 - 11
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	n.a.
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	p 10
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	n.a.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	n.a.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	p 12 - 14
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	p 14 - 17
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	p 16 - 17, p 18
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	p 19

		of methodological assumptions (such as discount rate, study perspective).	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	n.a.
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	n.a.
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	p 19 - 22
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	p 22
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	p 23

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.

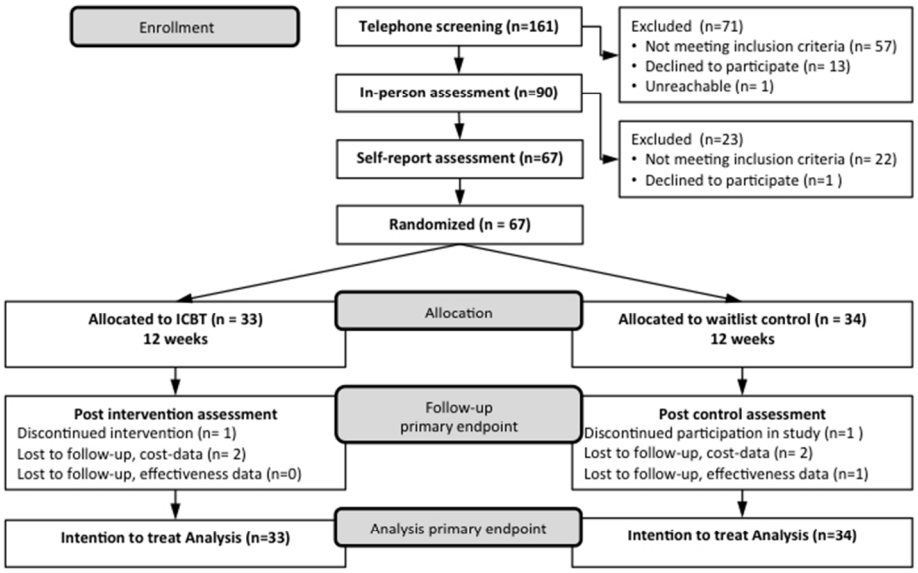

Figure 1

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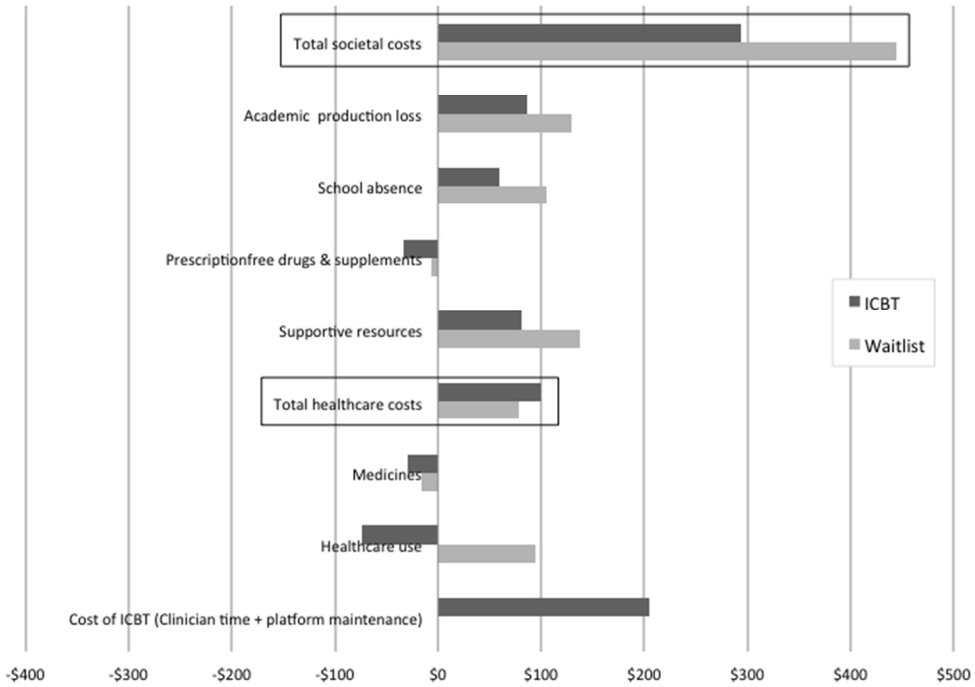

Figure 2

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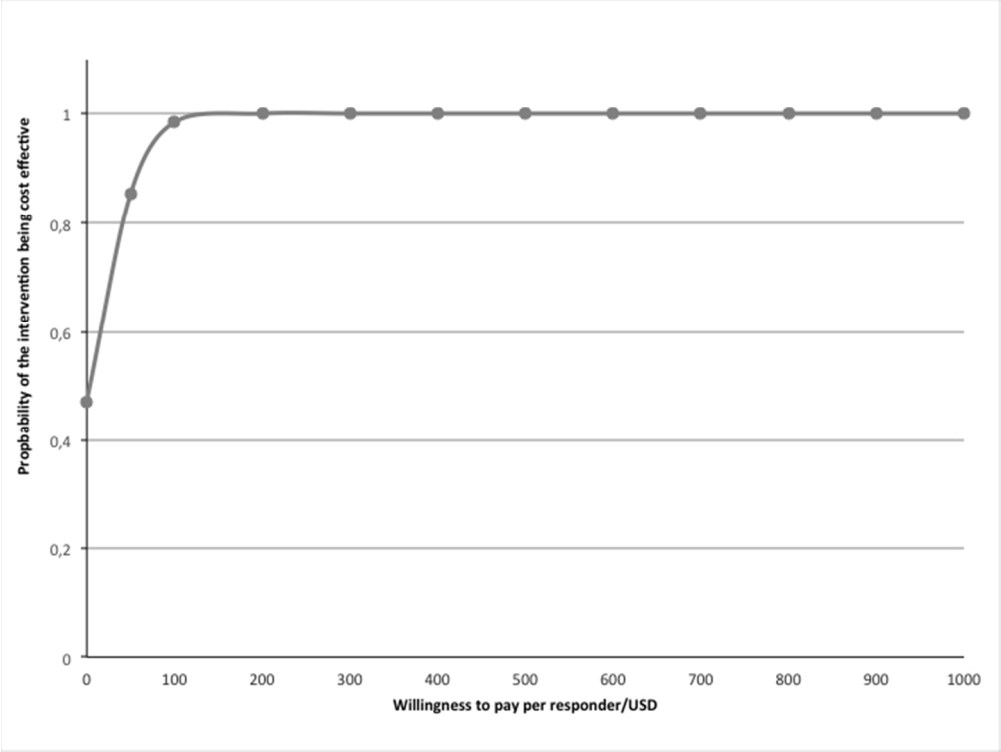
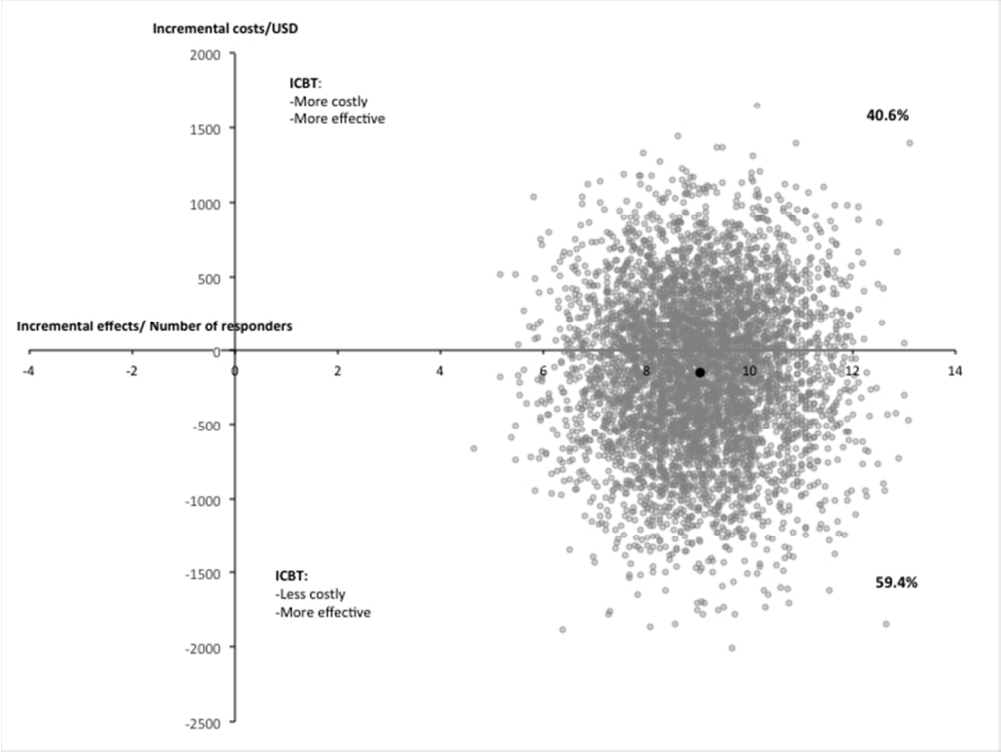


Figure 3

254x190mm (72 x 72 DPI)

Online supplement 1: Unit costs and sources

Item	Unit Cost (USD)	Source
Healthcare use (per visit)		
General practitioner (GP)	219.24	Sweden's Municipalities and Counties
Nurse	73.08	Sweden's Municipalities and Counties
Social worker	73.08	Sweden's Municipalities and Counties
Physiotherapist	73.08	Sweden's Municipalities and Counties
Specialist practitoner	385.13	Sweden's Municipalities and Counties
Chiroprator or osteopath	73.08	Sweden's Municipalities and Counties
Psychologist	73.08	Stockholm's County
Alternative medicine e.g acupuncture	73.08	Sweden's Municipalities and Counties
Medicines (Pharmaceuticals)		
Medication e.g anti-depressants	Individual product prices	Medical products agency of Sweden
Supportive resources		
Tutoring help (1 hour)	53.06	Sweden's Municipalities and Counties
Productivity loss		
Average salary/wage/hour in Sweden (2015)	31.31	Statistics Sweden
Cost of leisure time/hour	10.96	Johannesson et al. 1990
Cost/child/day for basic education	66.85	Swedish National Agency for Education
Intervention cost		
Maintenance cost (per patient)	65.08	Own estimate
ICBT clinician cost (per hour)	25.98	Average hourly psychologist wage, Statistics Sweden



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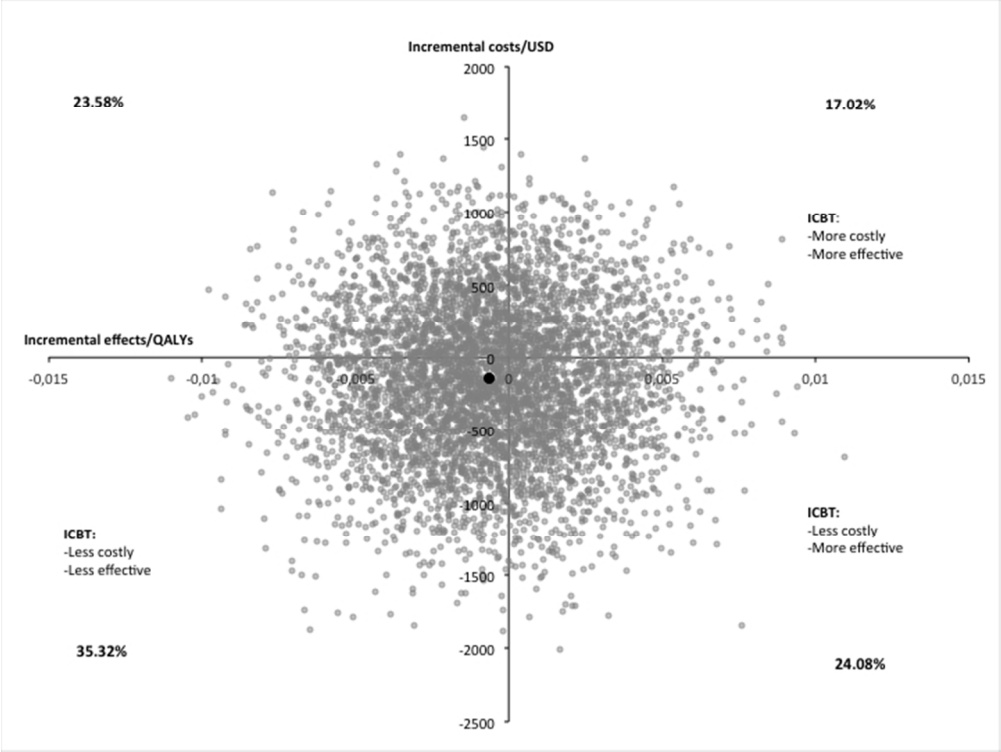

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BMJ Open

Cost-effectiveness of therapist-guided Internet-delivered Cognitive Behavior Therapy for pediatric Obsessive-Compulsive Disorder: Results from a Randomized Controlled Trial

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Primary Subject Heading:	Mental health
Secondary Subject Heading:	Health economics
Keywords:	Obsessive Compulsive Disorder, cognitive behavior therapy, Child & adolescent psychiatry < PSYCHIATRY, Telemedicine < BIOTECHNOLOGY & BIOINFORMATICS, HEALTH ECONOMICS

Cost-effectiveness of therapist-guided Internet-delivered Cognitive Behavior Therapy for pediatric Obsessive-Compulsive Disorder: Results from a Randomized Controlled Trial

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Keywords: Obsessive-compulsive disorder; cognitive behavior therapy; Internet; pediatric; cost-effectiveness

ABSTRACT

Objectives To evaluate the cost-effectiveness of a therapist-guided Internet-delivered cognitive behavior therapy (ICBT) intervention for adolescents with obsessive-compulsive disorder (OCD), compared to untreated patients on a waitlist.

Design Single-blinded randomized controlled trial.

Setting A research clinic within the regular child and adolescent mental health service in Stockholm, Sweden.

Participants Sixty-seven adolescents (12–17yrs) with a DSM-5 diagnosis of OCD.

Interventions Either a 12-week, therapist-guided ICBT intervention or a wait list condition of equal duration.

Primary outcome measures Cost data were collected at baseline and after treatment, including healthcare use, supportive resources, prescription drugs, prescription-free drugs, school absence and productivity loss, as well as the cost of ICBT. Health outcomes were defined as treatment responder rate and Quality Adjusted Life Years (QALYs) gain. Bootstrapped mixed model analyses were conducted comparing incremental costs and health outcomes between the groups, from the societal and healthcare perspectives.

Results Compared to waitlist control, ICBT generated substantial societal cost savings averaging -144.98USD (95% *CI* [-159.79, -130.16]) per patient. The cost reductions were mainly driven by reduced healthcare use in the ICBT group. From the societal perspective, the probability of ICBT being cost-saving compared to waitlist control was approximately 60%. From the healthcare perspective, the cost

per additional responder to ICBT compared to waitlist control was approximately 78 USD.

Conclusions The results suggest that therapist-guided ICBT is a cost-effective treatment and results in societal cost savings, compared to patients that do not receive evidence-based treatment. Since, at present, most patients with OCD do not have access to evidence-based treatments, the results have important implications for the increasingly strained national and healthcare budgets. Future studies should compare the cost-effectiveness of ICBT with regular face-to-face CBT.

Trial registration www.clinicaltrials.gov (NCT02191631)

STRENGTHS AND LIMITATIONS OF THIS STUDY

- Study strengths include a randomized controlled trial design and blinded assessors of the clinical outcome as well as robust statistical methods (mixed models in combination with bootstrapped sampling).
- In addition, cost analyses were conducted from a societal and healthcare perspective, including a wide range of cost variables.
- The study results are limited by a moderate sample size and measurements at two time points (before and after intervention).
- Bigger sample sizes, more frequent measurements and longer, controlled follow-up time points should be implemented in future replications to allow for broader generalizability.

INTRODUCTION

Obsessive-Compulsive disorder (OCD) is characterized by anxiety-provoking intrusive thoughts or urges (obsessions), coupled in most cases with excessive and ritualistic behaviors (compulsions) [1]. OCD has a prevalence between 0.25 to 2 % in the child and adolescent population [2,3] and is associated with substantial reductions in health-related quality of life [4,5], as well as impairments in education, social relations, and family functioning [6]. The societal cost of OCD in adults in the USA is estimated to 10.6 billion USD per year [7].

International guidelines, such as those published by the American Academy of Child and Adolescent Psychiatry [8] and NICE [9] recommend cognitive behavioral therapy (CBT) as the first line treatment for young people with OCD. CBT is effective for the majority of patients, with effect sizes averaging *g*=1.2 [10]. However, a majority of patients do not have access to high quality CBT [11], due to a range of reasons, including shortage of therapists, geographical barriers, limited availability of specialized care and patients' delayed help seeking [12,13]. To overcome these challenges, internet-delivered CBT (ICBT) has emerged as a treatment format that is not bound to temporal or geographic barriers [14]. In ICBT, the patient works with the same content and homework tasks as in traditional face-to-face CBT (for example, psychoeducation, exposure and response prevention, relapse prevention), the only difference being that the treatment is delivered entirely via the Internet. ICBT is most effective when patients receive support from a clinician [15,16]. Typically, the clinician communicates with the patients via asynchronous online messages, thus not requiring booked appointments. An advantage of ICBT, compared to other novel treatment formats that are delivered via web-camera [17] or telephone [18], is that it

does not require booked appointments and allows for a significant reduction of clinician times.

In adults, ICBT has been evaluated in over 100 randomized controlled trials (RCTs) for a range of different psychiatric conditions and results have shown effect sizes that were in the same range as those of face-to-face CBT [19]. The development of ICBT for the pediatric population however, has been lagging behind considerably, with currently only 19 randomized controlled trials in all psychiatric and somatic diagnostic domains [20]. Our research group has recently developed a therapist-guided ICBT protocol for pediatric OCD, which we initially evaluated in an open feasibility trial (*N*=21). Results showed significant and large improvements in OCD symptoms from pre- to post-treatment and high satisfaction with the treatment [21]. A subsequent RCT compared ICBT against a waitlist control in a group of 67 adolescents with OCD. Results showed that ICBT was highly acceptable and superior to a waitlist control [22]. Further, patients continued improving during the follow-up period. The average clinician support time was only 17.5 minutes per patient/week. Thus, ICBT has the potential to reduce treatment costs and being a cost-effective treatment due to its high degree of accessibility and reduced therapist contact.

Although ICBT has shown promise in terms of effectiveness in many mental health conditions, there have been few health economic evaluations. In a comprehensive review that included studies from the adult and child/adolescent ICBT field, only five of the 139 screened studies included a cost-effectiveness evaluation; three of those were excluded due to methodological issues, and none of the studies involved children/adolescents [23]. In adults with OCD, only three cost-

effectiveness evaluations have been conducted for computerized or Internet-based CBT. In one study comparing entirely self-guided, computer-aided CBT with standard face-to-face CBT and relaxation, computer-aided CBT was less effective than face-to-face CBT, but, given the lower therapist cost of this treatment, computer-aided CBT produced more benefit per unit cost [24]. In another study comparing therapist-guided ICBT with an online supportive therapy control condition [25], ICBT was a cost-effective treatment with an average cost of 931 USD for one additional treatment responder and 7186 USD per quality adjusted life year (QALY) gained. In a third study, Andersson et al. evaluated the cost-effectiveness of a post-treatment booster program in order to help patients maintain treatment gains after therapist-guided ICBT [26]. On average, the cost of one avoided relapse by providing booster ICBT vs. no additional treatment was estimated to be 1066-1489 USD. To our knowledge, there have been no previous studies evaluating the cost-effectiveness of ICBT for pediatric OCD.

This paper reports the cost-effectiveness of therapist-guided ICBT for adolescents with OCD, compared to a waitlist control condition, from both a societal as well as a healthcare perspective. We hypothesized that ICBT would result in a reduction in societal costs, originating from reduced health care utilization and increased academic functioning, amongst other indicators.

METHODS

Study design

Cost-effectiveness data was collected in tandem with a randomized controlled trial [22]. Adolescents (*N*=67) with OCD were randomized to either ICBT (*n*=33) or a waitlist control (*n*=34), each of 12 weeks duration. Assessment points for the data collection were pre-treatment and post-treatment. The assessors of the primary clinical outcome measure were blinded for group allocation. The trial design and study flow is presented in **Figure 1**. The study was approved by the Regional Ethical Review Board in Stockholm, Sweden (2014/673-31/2) and registered on clinicaltrials.gov (NCT02191631).

Study sample

Information about the study was provided via mental health care services, schools and newspaper advertisements. Patients were eligible if they were 12 to 17 years of age, fulfilled criteria for OCD [1] and had moderate to severe symptom severity (i.e. at least 16 points on the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) [27], were able to communicate in Swedish, had access to the internet and a parent to co-participate in the intervention. Patients on psychotropic medication were required to be on a stable dose for the last 6 weeks prior to baseline assessment. Comorbidity was allowed except for conditions with a different treatment indication e.g. autism spectrum disorder, psychosis, bipolar disorder, severe eating disorder, suicidal ideation, substance abuse. Patients that had completed CBT for OCD 12 months prior to baseline assessment or had an ongoing CBT treatment were excluded from the study. All included patients gave verbal and written informed consent for study participation. Information on the study sample is presented in Table 1. There were no statistically significant baseline differences between the ICBT and waitlist group.

Table 1: Patients' characteristics

	Control (*n* = 34)		ICBT (*n* = 33)		Total (*N* = 67)	
Sex (% girls)	41%		52%		46%	
Age (M, SD)	14,97	(1,66)	14,21	(1,69)	14,60	(1,71)
Country of birth (%)						
Sweden	88%		97%		93%	
Other European	6%		3%		4%	
Asian	6%		0%		3%	
Parent's educational level (%)						
Primary	0%		3%		1%	
High school	29%		21%		25%	
College	3%		6%		4%	
Vocational	6%		3%		4%	
University	50%		48%		49%	
Doctoral degree	0%		3%		1%	
Other	12%		15%		13%	
OCD symptom severity baseline score, CY-BOCS (M, SD)	22,12	(3,91)	23,00	(4,31)	22,55	(4,10)
Number of comorbid diagnoses (%)						
0	53%		61%		57%	
1	35%		21%		28%	
2	9%		9%		9%	
3	3%		6%		4%	
4	0%		3%		1%	
Medication (on-going)						
None	82%		72%		78%	
SSRI	18%		18%		18%	
Stimulants	3%		6%		4%	
Tricyclic antidepressants	0%		3%		1%	
Type of referral						
Self-referral	91%		94%		93%	
CAMHS referral	9%		6%		7%	

Abbreviations: ICBT = internet-delivered cognitive behavior therapy; OCD = obsessive-compulsive disorder; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; SSRI = Selective serotonin reuptake inhibitor; CAMHS = Child and Adolescent Mental Health Service

Intervention

The ICBT intervention, “BiP OCD”, has been previously tested in an open feasibility trial [21,28] and recently in a 12-week waitlist-controlled RCT [22]. BiP OCD is a web-based, therapist-guided and parent-assisted CBT intervention with treatment components in line with clinical expert guidelines for OCD treatment, namely psychoeducation, exposure with response prevention, cognitive restructuring and relapse prevention [29]. The treatment content is age-tailored for 12 to 17 year olds with texts to read, short videos to watch and exercises to work with. The treatment content is presented in 12 chapters that are consecutively unlocked by the patient. A clinical psychologist provides asynchronous written feedback 5 days a week via messages through the secure Internet portal, and occasionally via telephone calls. Adolescents access their personal content via password and text-message secured login. Parents participate in the treatment through parent-specific chapters, with varying degrees of parental involvement depending on the child’s age. A more detailed description of BiP OCD can be found elsewhere [21,22,28].

During the 12-week study period, patients on the waitlist control were allowed to continue any medication and psychosocial care except those specified in the exclusion criteria for the study (ongoing CBT).

Economic evaluation

Health economics is the application of economics principles on health and healthcare [30]. Cost-effectiveness analysis is a branch of health economics concerned with the comparative analysis of the incremental differences in costs and effects of alternative interventions for a given health condition. The result of the

analysis is usually presented as an incremental cost-effectiveness ratio (ICER), where the difference in costs is divided by the difference in effects [31].

The economic evaluation framework of this study was a within trial cost-effectiveness analysis undertaken from a societal perspective (including costs associated with healthcare, education and individual patients) and, separately, a healthcare perspective (including only costs associated with healthcare).

The time horizon was 12 weeks, which mirrors the duration of the intervention. Costs were collected in tandem with our RCT in Swedish Krona (SEK, 2014) and presented in US dollars (USD, 2016) using the purchasing power parity (PPP) estimates [32].

Costs

Two categories of costs were estimated, costs for the ICBT intervention and other societal costs involving costs that arose on the side of the healthcare and educational system as well as costs that arose for patients directly.

Intervention costs included cost for the clinicians' time for the 12 weeks of ICBT as well as ICBT treatment platform maintenance costs. Clinician times were logged for every clinician's contact with individual patients and included writing messages to the patients and telephone calls. The clinician time spent on each individual patient was then multiplied by the average hourly psychologist wage (**Supplementary table S1**). On average, the clinicians spent 17.5 minutes per patient/week. Maintenance costs consisted of external IT support, technical upgrades and iterative development of platform functionality. The maintenance costs were in total 4390.4 USD for 12 weeks of the intervention, or 65.60 USD as a fixed cost per ICBT patient.

Other societal costs were collected using an adapted version of the parent-rated Trimbos Questionnaire for Costs associated with Psychiatric Illness (TiC-P) [33] at baseline and post-treatment. The questionnaire includes items on healthcare resource use (e.g. medical doctor or psychologist visits), supportive resources (e.g. private tutoring), medications, prescription-free drugs or supplements, absenteeism from school and academic productivity loss when being at school despite not feeling well. Information on parental productivity loss was also collected, but due to an error in the wording of the questionnaire, that information could not be used in the analyses. Costs were estimated by the product of unit costs and frequencies, e.g. costs for doctors' visits*number of visits.

The analytic approach used in this study was to estimate the full cost change of the 12 weeks of ICBT or waitlist. A limitation of the TIC-P is however that it captures merely the last four weeks. As the study period was 12 weeks, using only the week 0 and week 12 measurement points would consequently have neglected the costs of week 4 and week 8. We therefore calculated the costs of weeks 4 and 8 using linear interpolation (following the notion that OCD symptoms change linearly over time [34], and that costs would follow the same trajectory). Consequently, the changes in costs were calculated as the accumulated sums of week 4, 8 and 12 costs with week 0 set to zero, and by that covering the whole study period while controlling for baseline differences. In a last step, we calculated the differences between the changes in costs of ICBT and the waitlist control, with positive values indicating additional costs of ICBT over the 12 weeks, compared to waitlist, and negative values indicating additional cost savings of ICBT compared to waitlist.

Unit costs and their sources are displayed in **supplementary table S1**, resource use is displayed in **supplementary table S2**.

Intervention costs and other societal costs were summed up to *total societal costs*. Further, intervention costs, costs for healthcare utilization and medications were summed up to *total healthcare costs*.

Health outcomes

The primary health outcome was defined as "treatment responder rate". In line with expert consensus [35], patients were classified as responders if they had shown a decrease of symptoms on the CY-BOCS of at least 35% at post-treatment and had a clinical global improvement rating (CGI-I) [36] of 1="very much improved" or 2="much improved".

The secondary health outcome was defined as gains in quality adjusted life years (QALYs). Patients filled in the European Quality of life Five Dimensions Questionnaire Youth version (EQ-5D-Y), to assess health-related quality of life [37]. EQ-5D is a widely used measure in health economic evaluations and consists of 5 dimensions measuring health-related functioning and quality of life i.e. pain/discomfort, anxiety/depression, self-care, mobility and usual activities. It also consists of a 0 - 100 visual analogue scale (VAS) used to measure subjective ratings of health. The EQ-5D-Y was chosen given the study sample age (12-17 years) and had previously shown feasibility of use in a Swedish pediatric population [38]. The health profiles derived from the EQ-5D-Y were used to estimate quality of life adjusted life years (QALYs), ranging from 0 to 1, with 1 representing one year of perfect health. The Swedish EQ-5D adult population value sets were used as a proxy in the calculation of QALYs [39], given that the adolescent value sets are not

yet available. The change in QALYs was then corrected for the intervention period expressed in years (i.e. 3 months = 0.25 of a year).

Statistical analyses

The pre-treatment differences in costs were tested using non-parametric Mann-Whitney tests. Treatment effects on responder rates between ICBT and waitlist were analyzed using Fisher's exact test while incremental differences in QALYs and costs between the intervention and waitlist control groups over time were analyzed using mixed effects models. Mixed effects models are equipped to analyze longitudinal data and are effective in handling of missing data [40], thus were deemed fit for these analyses. Since the cost data were skewed (Shapiro-Wilk test of normality $z=7.05$, $p<.001$), mixed models analyses were carried out with 5000 non-parametric bootstrap samplings to create normally distributed mean values for further analyses.

Cost-effectiveness analyses

Two types of cost-effectiveness analyses were conducted: a cost-effectiveness analysis using responder rates as the primary health outcome and a cost-utility analysis using QALYs as a secondary health outcome. An incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in total costs by the difference in responder rate, as well as in QALYs, between the ICBT and waitlist groups.

The bootstrapped results, pairings of the differences in costs with the differences in health outcomes, were represented visually on a cost-effectiveness plane **(supplementary figures S3 and S4)**. The cost-effectiveness plane depicts the uncertainty around the cost-effectiveness estimate, the ICER. The horizontal axis divides the plane according to incremental effect and the vertical axis according to

incremental societal cost, which divides the plane into four different quadrants. Iterations plotted in the top right quadrant are those where the intervention is more effective and more costly than the comparator; those in the bottom right quadrant are more effective and less costly; those in the bottom left quadrant are less effective and less costly; and those in the top left quadrant are more costly and less effective [31]. To analyze the cost-effectiveness from a healthcare perspective, the ICER was estimated, comparing the differences in total healthcare costs and health outcomes between the ICBT group and waitlist control group. The probability of ICBT to be cost-effective was calculated, given different willingness-to-pay scenarios, presented visually by means of a cost-effectiveness acceptability curve (CEAC) produced using the net-benefit approach, i.e. (λ x E) – ΔC where λ is the willingness to pay (i.e. the cost that the society is willing to pay for one unit of improvement), E is the health benefit and ΔC is the change in costs **(Figure 3)**.

The statistical significance was set at a p-value of 0.05 and 95% confidence intervals (*CI*). The calculations were done using STATA version 13 (StataCorp) and Excel 2013 (Microsoft).

Sensitivity analyses

A sensitivity analysis was carried out to test three scenarios that were thought to influence the final results. Firstly, we re-ran the cost-utility analysis using EQ-5D-Y VAS scores instead of the estimated EQ-5DY profile QALYs. This was because the QALYs used in the primary analysis were determined using an adult value set algorithm as the adolescent value-set was not yet available, thus a potential estimation error. Secondly, we calculated the correlations between EQ-5D-Y QALYs estimates, EQ-5D-Y VAS scores and the responder status in the study patients. This

was to test whether the different outcome measures were strongly associated with each other, which would further strengthen the validity of the measures. Lastly, we repeated the cost-effectiveness analyses with the intervention costs increased by 50% in order to cater for changes in ICBT platform maintenance and clinician time costs, thus testing the robustness of the cost-effectiveness result given inflated costs.

RESULTS

Costs

The mean intervention cost per ICBT patient was estimated as maintenance costs of 65.98 USD and clinician's time of 121.39 USD, i.e. a total of 187.37 USD per patient (bootstrapped estimate of 196.66 USD).

There were no total societal cost differences between the two groups at baseline (z=-1.09, p=.28). After treatment, the average overall societal cost difference between ICBT and waitlist control was M=-144.98 USD (95% CI [- 159.79, -130.16]) per patient, indicating cost savings of ICBT compared to waitlist. There was an increase of healthcare use (i.e. clinician visits) in the waitlist control compared to intervention group resulting in a M=-162.21 USD difference (95% CI [- 173.32, -151.32]), which was the main driver of the overall cost difference. The average total healthcare cost difference was M=21 USD per patient, indicating additional costs of ICBT compared to waitlist.

For a complete presentation of baseline costs and cost changes over the 12-week intervention period, see **Table 2.** For differences in cost changes see **Figure 2**.

Table 2: Estimated baseline and pre- to post-intervention change scores for societal costs, intervention costs and health outcomes, per patient

		Baseline				Pre- to post-intervention					
		ICBT		Waitlist		ICBT		Waitlist		Cost-difference ICBT vs waitlist*	
		Mean	95% CI	Mean	95% CI	Mean change	95% CI	Mean change	95% CI	Mean difference	95% CI
ICBT intervention costs	Clinician time & platform maintenance	-	-	-	-	196.66	196.33-196.98	0	0	196.66	196.33-196.98
Other societal costs	Healthcare use	425.66	237.08-614.25	323.63	190.75-456.50	-71.21	-79.86 - -62.58	90.99	84.42-97.57	-162.21	-173.32 - -151.32
	Medicines	32.20	13.77-51.58	18.66	0 - 38.28	-28.88	-29.74 - -28.01	-15.80	-16.64 - -14.97	-13.07	-14.27 - -11.88
Total health care costs		**457.86**	**261.30-654.42**	**342.29**	**208.78-475.79**	**96.57**	**87.56-105.56**	**75.19**	**68.56-81.82**	**20.57**	**9.78-31.36**
	Supportive resources	48.09	-0.97-98.11	16.24	-0.52-33.01	78.52	75.97-81.06	132.77	131.39-134.15	-54.25	-57.13 - -51.37
	Prescription-free drugs & supplements	19.06	-11.72-50.80	8.97	1.41-16.50	-32.47	-33.83 - -31.11	-6.62	-6.96 - -6.28	-25.85	-27.26 - -24.45
	School absence	129.47	25.34-233.60	70.02	36.29-103.77	56.82	52.09-61.55	101.25	99.02-103.48	-44.43	-49.65 - -39.06
	Academic production loss	43.87	8.46-79.28	32.74	-4.88-70.37	83.04	80.83-85.25	125.13	123.01-127.25	-42.09	-45.12 - -39.21
Total societal costs		**698.36**	**421.51-975.21**	**470.26**	**317.41-623.11**	**282.74**	**270.30-295.17**	**427.72**	**419.57-435.86**	**-144.98**	**-159.79 - -130.16**

Health outcomes	Number of Treatment responders (%)	-	-	-	-	27%	20-35%	0%	0%	27%	20-35%
	QALYs	.95	.95 - .96	.96	.95 - .97	-.0015#	-.005- -.0025	-.00075	-.005- - .0025	-.00065	-.00073 - -.00056
	VAS	66.11	58.60 - 73.61	66.20	58.80 - 73.59	.0007#	-.0168- .0181	-.0034	-.0169 - .0104	.0041	.0034-.0049

Note: # = Values have been multiplied with the adjustment factor of the intervention period of 3 months/one year i.e. 0.25; * = negative values indicating cost-savings of ICBT compared to waitlist.
Abbreviations: ICBT=Internet-delivered Cognitive Behavior Therapy, CI=Confidence interval

Health outcomes

At post-intervention, there were nine (27%) strictly defined treatment responders in the ICBT group and none in the waitlist (Fisher's exact test, *p*=.001). There were no significant time*group effects in EQ-5D-Y estimated QALYs (*B*=.000, *z*=.01, *p*=.99) or in the EQ-5D-Y VAS scores (*B*=1.69, *z*=0.38, *p*=.71).

Cost-effectiveness analyses

The distribution of total societal cost differences and differences in treatment response of the bootstrapped estimations were centered in the south-east quadrant of the cost-effectiveness plane, indicating dominance of ICBT over waitlist (less costly and more effective), see **supplementary figure S3**. Accordingly, the probability of ICBT to be cost saving was 59.4 percent. The distribution of cost differences and differences of QALYs were centered south of the midline at the origin, indicating less costs of ICBT but equal effect compared to waitlist, see **supplementary figure S4**.

When analyzing cost effectiveness from a healthcare perspective, (i.e. Healthcare costs = cost of ICBT + medicines + healthcare use), the incremental cost effectiveness ratio (ICER) was estimated to 78 USD per responder. Considering a range of willingness-to-pay scenarios, the probability of ICBT to be cost-effective approximated 100% at 4000 USD per responder (see cost-effectiveness acceptability curve in **Figure 3**).

Sensitivity analyses

Using the VAS scores instead of EQ-5D-Y estimated QALYs showed a minimal, non-significant increase of the ICBT group compared to the waitlist at the post-intervention assessment (**Table 2**) with *B*=1.69, *z*=0.38, *p*=.71.

The correlation between responder status and EQ-5D-Y estimated QALYs was examined, but found to be very low and non-significant (*r*=.16, *p*=.23). The correlation between responder status and VAS ratings was in the same range and non-significant (*r*=.18, *p*=.16). The correlation of EQ-5D-Y estimated QALYs and EQ-5D-Y VAS ratings was significant and in the small to moderate range (*r*=.27, *p*=.04).

When repeating the analysis with intervention costs raised by 50% to account for a scenario with increased maintenance and clinician expenses, the total cost difference was reduced to *M*=- 46.92 USD (95% *CI*[- 61.74, - 32.11]) per patient, however, ICBT was still cost saving compared to waitlist control.

DISCUSSION

To our knowledge, this is the first study to evaluate the cost-effectiveness of therapist-guided ICBT for pediatric OCD and one of the very few in the field of child and adolescent ICBT. The results indicated that ICBT is not only clinically superior but also results in cost savings, compared to leaving OCD patients untreated. ICBT resulted in societal cost savings of about 145 USD per patient and had an incremental response rate of 27%. The cost saving effects of ICBT were still observed when conservatively increasing the intervention cost by 50%. The main driver of the cost savings was a marked reduction in healthcare utilization in the ICBT group, with a mean cost saving of 162 USD in the ICBT group compared to the waitlist control. From a healthcare perspective, ICBT was cost effective compared to

the waitlist control with an average additional cost of 78 USD/responder. The probability of the intervention being cost effective plateaued at 100% when the willingness to pay was greater than 4000 USD/responder.

In light of the current cost developments, it is evident that mental healthcare increasingly strains national budgets. In the US over 300 billion dollars per year are spent on mental health considering disability benefits, healthcare costs and lost earnings [41]. Sweden, where the study was conducted, is no exception; 10.5 billion USD are spent per year on mental health disorders [42,43]. Consequently, efficient use of limited resources has become an important step in the evaluation of new treatments. In this context, this study makes an important contribution to the field in general and to the field of pediatric OCD in particular. The finding that therapist-guided ICBT is a cost-effective treatment and results in societal cost savings, compared to leaving patients untreated, suggests that integrating ICBT within regular child and adolescent psychiatry could address several of the existing treatment gaps. Furthermore, as the risk for not receiving effective treatment is most significant in developing countries [44], the potential benefits of cost-saving interventions with minimal resource requirements might be even higher in those regions. One possible way to maximize the cost-saving potential of ICBT could be to offer ICBT as a first step in a stepped care model, thus freeing resources for more complex cases. Studies that evaluate such a stepped care approach, including a cost-evaluation of the different steps, are warranted.

Unexpectedly, ICBT did not yield any effects on QALYs. Sensitivity analyses revealed that both measures of QALYs (EQ-5D-Y health profiles and EQ-5D-Y VAS scores) were not correlated with the clinical outcome, and only weakly correlated

with one another. This raises the question of whether the EQ-5D-Y is a suitable quality of life measure for our patient group. Previous studies were able to demonstrate a clear association of OCD symptoms with decreased quality of life,[4] as well as changes in quality of life following treatment for OCD.[5] However, those studies did not use the EQ-5D-Y. Because the scale's individual items are more focused on somatic aspects of quality of life, such as mobility and pain, it might not accurately represent quality of life gains that are associated with reduced OCD symptoms. Notably, the utility values pre-intervention were already in the high range of the scale i.e. 0.95, and thus it is likely that a ceiling effect occurred. Furthermore, in absence of available norms for Swedish adolescents, we applied an adult algorithm in order to calculate QALYs. Consequently, future evaluations in this field should choose quality of life measures that are validated, appropriate for the patient population and sensitive to change.

Our results need to be interpreted in light of some study limitations. Firstly, the study is based on a modestly sized sample and, as the cost-effectiveness planes show, there is some uncertainty about the precision of the estimates. The results should therefore to be seen as preliminary and need replication in a larger sample. Secondly, the societal costs were collected at baseline and post-treatment and were interpolated for time period in between, on the assumption that they varied linearly over time. Future evaluations should employ more frequent cost measurements, covering the whole treatment and follow-up period. Thirdly, the study period covered only the short-term outcomes from the 12-week intervention phase. As the benefits of ICBT continue beyond the acute phase of the treatment and into the follow-up [21,22], a longer evaluation time frame would be appropriate and may possibly result in additional cost savings. Future studies should therefore extend the time frame to

at least 3 months after treatment. Fourthly, due to an error, cost estimates about parental productivity loss could not be included. As it can be assumed that parental psychosocial and occupational functioning would be affected by the child's OCD symptoms, it could be possible that our results underestimate the true cost associated with OCD. Another limitation is the choice of control group. As most OCD patients do not receive CBT, the waiting-list comparator could still be regarded as an ecologically valid control condition. However, further evaluations should include comparisons with the gold standard treatment of pediatric OCD, face-to-face CBT. As the current study shows somewhat lower response rates than those found in face-to-face treatment [10], it is conceivable that ICBT may be less effective than face-to-face CBT, but still result in substantial cost savings. Finally, the majority of patients were self-referred and an increased proportion of highly educated parents could indicate a selected sample, and results may therefore not generalize fully to patient populations that typically are found within mental health care.

To summarize, the results of this study show that therapist-guided ICBT is cost-effective compared to no treatment. Given the limitations of the current study, the results should be replicated in larger samples, employing more adequate measures of health-related quality of life, optimized cost measurements and longer follow-up periods to better capture both costs and health outcomes over time. Furthermore, a direct head-to-head comparison of therapist-guided ICBT with standard face-to-face CBT would be informative, as ICBT is hypothesized to generate cost savings compared to face-to-face CBT, even if ICBT were found to be less efficacious. Non-inferiority and stepped-care designs, combined with robust health economic evaluations should provide useful information for the design and optimization of specialist OCD clinics and child and adolescent psychiatry services in general.

AUTHORS' CONTRIBUTIONS

Mr Lenhard contributed to the conception and design of the study, data collection, trial management, analysis and interpretation of the data, and drafting the article. Mr Ssegonja and Drs Andersson and Feldman contributed to the statistical analyses and interpretation of the data. Drs Andersson, Mataix-Cols, Rück and Serlachius contributed to the conception and design of the study and interpretation of the data. All authors were involved in revising the manuscript critically for important intellectual content, and approved the final version.

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REFERENCES

1 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, DSM 5*. 5th ed. Arlington, VA: : American Psychiatric Publishing 2013.

2 Heyman I, Fombonne E, Simmons H, *et al.* Prevalence of obsessive-compulsive disorder in the British nationwide survey of child mental health. *Int Rev Psychiatry* 2003;**15**:178–84. doi:10.1080/0954026021000046146

3 Valleni-Basile LA, Garrison CZ, Jackson KL, *et al.* Frequency of obsessive-compulsive disorder in a community sample of young adolescents. *J Am Acad Child Adolesc Psychiatry* 1994;**33**:782–91. doi:10.1097/00004583-199407000-00002

4 Lack CW, Storch EA, Keeley ML, *et al.* Quality of life in children and adolescents with obsessive-compulsive disorder: base rates, parent–child agreement, and clinical correlates. *Soc Psychiatry Psychiatr Epidemiol* 2009;**44**:935–42. doi:10.1007/s00127-009-0013-9

5 Weidle B, Jozefiak T, Ivarsson T, *et al.* Quality of life in children with OCD with and without comorbidity. *Health Qual Life Outcomes* 2014;**12**:152. doi:10.1186/s12955-014-0152-x

6 Piacentini J, Bergman RL, Keller M, *et al.* Functional impairment in children and adolescents with obsessive-compulsive disorder. *J Child Adolesc*

Psychopharmacol 2003;**13 Suppl 1**:S61–9. doi:10.1089/104454603322126359

7 Eaton WW, Martins SS, Nestadt G, *et al.* The burden of mental disorders. Epidemiol. Rev. 2008;**30**:1–14. doi:10.1093/epirev/mxn011

8 Geller DADA, March JSJ, Psychiatry AA of C and A, *et al.* Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2012;**51**:98–113. doi:10.1016/j.jaac.2011.09.019

9 NICE. Obsessive-Compulsive Disorder: Core Interventions in the Treatment of Obsessive-Compulsive Disorder and Body Dysmorphic Disorder (clinical guideline 31). 2005.http://www.nice.org.uk/guidance/CG31 (accessed 18 Dec2012).

10 McGuire JF, Piacentini J, Lewin AB, *et al.* A Meta-Analysis of Cognitive Behavior Therapy and Medication for Child Obsessive-Compulsive Disorder: Moderators of Treatment Efficacy, Response, and Remission. *Depress Anxiety* 2015;**32**:580–93. doi:10.1002/da.22389

11 Goodwin R, Koenen KC, Hellman F, *et al.* Helpseeking and access to mental health treatment for obsessive-compulsive disorder. *Acta Psychiatr Scand* 2002;**106**:143–9. doi:10.1034/j.1600-0447.2002.01221.x

12 Simonds LM, Thorpe SJ. Attitudes toward obsessive-compulsive disorders--an experimental investigation. *Soc Psychiatry Psychiatr Epidemiol* 2003;**38**:331–6. doi:10.1007/s00127-003-0637-0

13 O'Neill J, Feusner JD. Cognitive-behavioral therapy for obsessive compulsive disorder: Access to treatment, prediction of long-term outcome with neuroimaging. Psychol. Res. Behav. Manag. 2015;**8**:211–23. doi:10.2147/PRBM.S75106

14 Andersson G. Using the Internet to provide cognitive behaviour therapy. *Behav Res Ther* 2009;**47**:175–80. doi:10.1016/j.brat.2009.01.010

15 Cuijpers P, Donker T, van Straten A, *et al.* Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies. *Psychol Med* 2010;**40**:1943–57. doi:10.1017/S0033291710000772

16 Cuijpers P, Donker T, Johansson R, *et al.* Self-guided psychological treatment for depressive symptoms: A meta-analysis. *PLoS One* 2011;**6**. doi:10.1371/journal.pone.0021274

17 Comer JS, Furr JM, Cooper-Vince CE, *et al.* Internet-Delivered, Family-Based Treatment for Early-Onset OCD: A Preliminary Case Series. *J Clin Child Adolesc Psychol* 2013;:1–14. doi:10.1080/15374416.2013.855127

18 Turner CM, Mataix-cols D, Lovell K, *et al.* Telephone Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Non-inferiority Trial. *J Am Acad Child Adolesc Psychiatry* 2014;**53**:1298–307.e2. doi:10.1016/j.jaac.2014.09.012

19 Hedman E, Ljótsson B, Lindefors N. Cognitive behavior therapy via the Internet: a systematic review of applications, clinical efficacy and cost-effectiveness. *Expert Rev Pharmacoecon Outcomes Res* 2012;**12**:745–64.

doi:10.1586/erp.12.67

20 Vigerland S, Lenhard F, Bonnert M, *et al.* Internet-delivered cognitive behavior therapy for children and adolescents: A systematic review and meta-analysis. *Clin Psychol Rev* 2016;**50**:1–10. doi:10.1016/j.cpr.2016.09.005

21 Lenhard F, Vigerland S, Andersson E, *et al.* Internet-delivered cognitive behavior therapy for adolescents with obsessive-compulsive disorder: An open trial. *PLoS One* 2014;**9**:e100773. doi:10.1371/journal.pone.0100773

22 Lenhard F, Andersson E, Mataix-Cols D, *et al.* Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Trial. *J Am Acad Child Adolesc Psychiatry* 2017;**56**:10–9.e2. doi:10.1016/j.jaac.2016.09.515

23 Arnberg FK, Linton SJ, Hultcrantz M, *et al.* Internet-delivered psychological treatments for mood and anxiety disorders: a systematic review of their efficacy, safety, and cost-effectiveness. *PLoS One* 2014;**9**:e98118. doi:10.1371/journal.pone.0098118

24 McCrone P, Marks IM, Greist JH, *et al.* Cost-effectiveness of computer-aided behaviour therapy for obsessive-compulsive disorder [1]. Psychother. Psychosom. 2007;**76**:249–50. doi:10.1159/000101504

25 Andersson E, Hedman E, Ljótsson B, *et al.* Cost-effectiveness of internet-based cognitive behavior therapy for obsessive-compulsive disorder: Results from a randomized controlled trial. *J Obsessive Compuls Relat Disord* 2015;**4**:47–53. doi:10.1016/j.jocrd.2014.12.004

26 Andersson E, Ljótsson B, Hedman E, *et al.* Cost-effectiveness of an internet-based booster program for patients with obsessive–compulsive disorder: Results from a randomized controlled trial. *J Obsessive Compuls Relat Disord* 2015;**4**:14–9. doi:10.1016/j.jocrd.2014.10.002

27 Scahill L, Riddle MA, McSwiggin-Hardin M, *et al.* Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry* 1997;**36**:844–52. doi:10.1097/00004583-199706000-00023

28 Lenhard F, Vigerland S, Engberg H, *et al.* 'On My Own, but Not Alone' - Adolescents' Experiences of Internet-Delivered Cognitive Behavior Therapy for Obsessive-Compulsive Disorder. *PLoS One* 2016;**11**:e0164311. doi:10.1371/journal.pone.0164311

29 Franklin ME, Foa EB. Treatment of obsessive compulsive disorder. *Annu Rev Clin Psychol* 2011;**7**:229–43. doi:10.1146/annurev-clinpsy-032210-104533

30 Morris, Stephen A.; Devlin, Nancy; Parkin, David & Spencer A. *Economic Analysis in Healthcare*. 2nd ed. New Jersey: : Wiley 2012. https://books.google.se/books/about/Economic_Analysis_in_Healthcare.html?id=Co-JZwEACAAJ&pgis=1

31 Drummond MF, Sculpher MJ, Torrance GW, *et al. Methods for the economic evaluation of health care programmes*. 2005. http://econpapers.repec.org/RePEc:oxp:obooks:9780198529453

32 CCEMG, EPPI. CCEMG - EPPI-Centre Cost Converter. 2016.http://eppi.ioe.ac.uk/costconversion/default.aspx

33 Bouwmans C, De Jong K, Timman R, *et al.* Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TiC-P). *BMC Health Serv Res* 2013;**13**:217. doi:10.1186/1472-6963-13-217

34 Andersson E, Enander J, Andrén P, *et al.* Internet-based cognitive behaviour therapy for obsessive-compulsive disorder: a randomized controlled trial. *Psychol Med* 2012;**42**:2193–203. doi:10.1017/S0033291712000244

35 Mataix-Cols D, De La Cruz LF, Nordsletten AE, *et al.* Towards an international expert consensus for defining treatment response, remission, recovery and relapse in obsessive-compulsive disorder. *World Psychiatry* 2016;**15**:80–1. doi:10.1002/wps.20299

36 Guy W. *Assessment manual for psychopharmacology, revised*. Washington DC: : US Government Printing Office 1976.

37 Wille N, Badia X, Bonsel G, *et al.* Development of the EQ-5D-Y: A child-friendly version of the EQ-5D. *Qual Life Res* 2010;**19**:875–86. doi:10.1007/s11136-010-9648-y

38 Burström K, Bartonek Å, Broström EW, *et al.* EQ-5D-Y as a health-related quality of life measure in children and adolescents with functional disability in Sweden: testing feasibility and validity. *Acta Paediatr* 2014;**103**:426–35. doi:10.1111/apa.12557

39 Burström K, Sun S, Gerdtham UG, *et al.* Swedish experience-based value sets for EQ-5D health states. *Qual Life Res* 2014;**23**:431–42. doi:10.1007/s11136-013-0496-4

40 Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing repeated-measures data and its reflection in papers published in the Archives of General Psychiatry. *Arch Gen Psychiatry* 2004;**61**:310–7. doi:10.1001/archpsyc.61.3.310

41 Kessler RC, Heeringa S, Lakoma MD, *et al.* Individual and societal effects of mental disorders on earnings in the United States: results from the national comorbidity survey replication. *Am J Psychiatry* 2008;**165**:703–11. doi:10.1176/appi.ajp.2008.08010126

42 OECD. *Mental Health and Work: Sweden*. OECD Publishing 2013. doi:10.1787/9789264188730-en

43 Tiainen A, Rehnberg C. The economic burden of psychiatric disorders in Sweden. *Int J Soc Psychiatry* 2010;**56**:515–26. doi:0020764009106140 [pii]\n10.1177/0020764009106140

44 Kohn R, Saxena S, Levav I, *et al.* The treatment gap in mental health care. *Bull World Health Organ* 2004;**82**:858–66. doi:/S0042-96862004001100011

FIGURES & ONLINE SUPPLEMENTS

Figure 1: Study flow chart

Figure 2: Mean cost-changes from baseline to post-treatment for ICBT and waitlist (USD)

Figure 3: Cost-effectiveness acceptability curve

Supplementary table S1: Unit costs and sources

Supplementary table S2: Resource use at pre- and post-intervention

Supplementary figure S3: Cost-effectiveness plane with bootstrapped differences in costs and response rates (black dot represents mean estimate)

Supplementary figure S4: Cost-effectiveness plane with bootstrapped differences in costs and QALYs (black dot represents mean estimate)

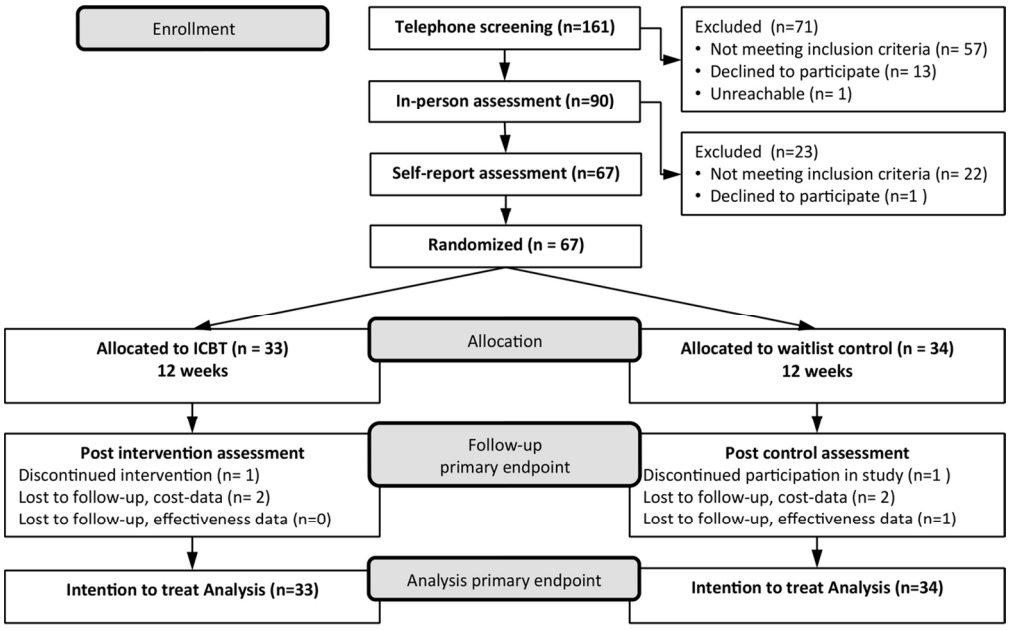

Figure 1: Study flow chart
Figure 1
119x73mm (300 x 300 DPI)

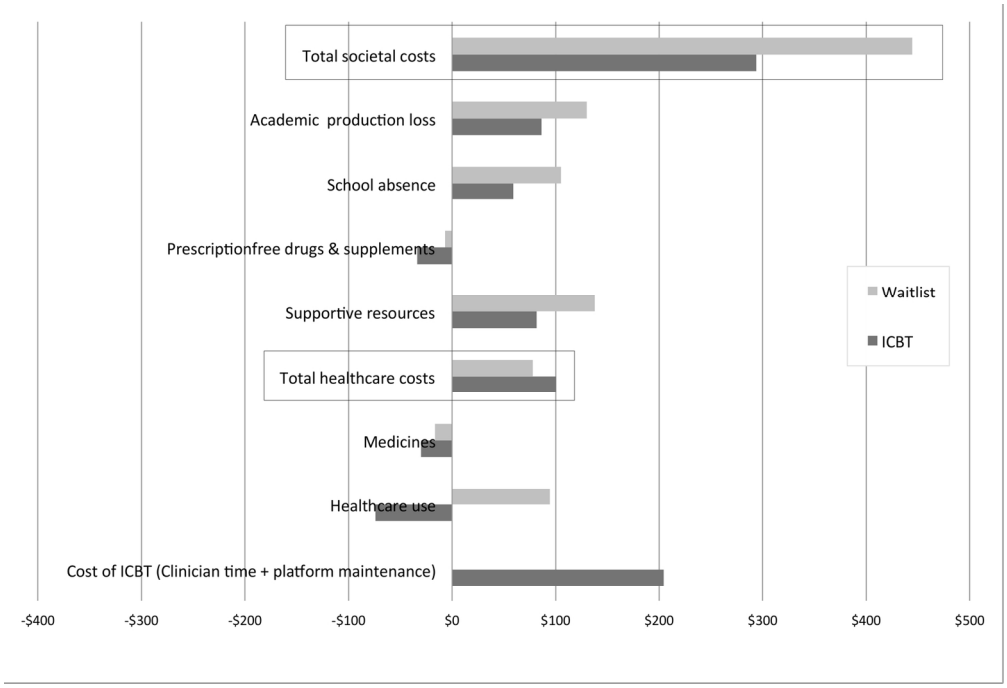

Figure 2: Mean cost-changes from baseline to post-treatment for ICBT and waitlist (USD)
Figure 2
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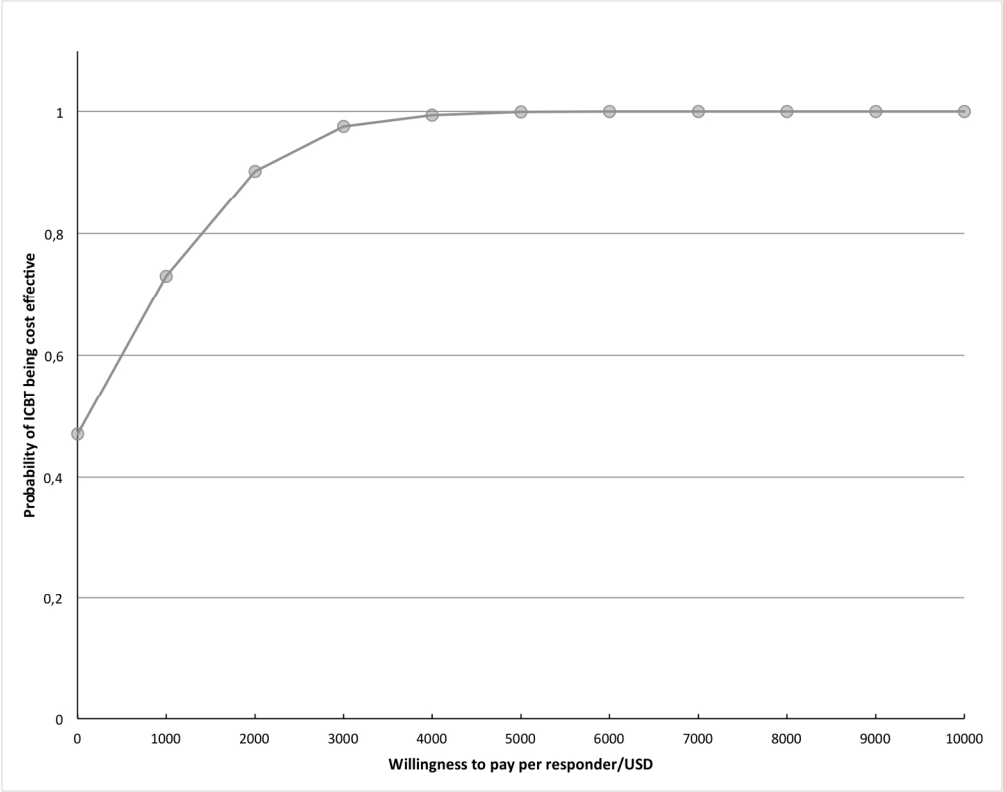


Figure 3: Cost-effectiveness acceptability curve
Figure 3
169x133mm (300 x 300 DPI)

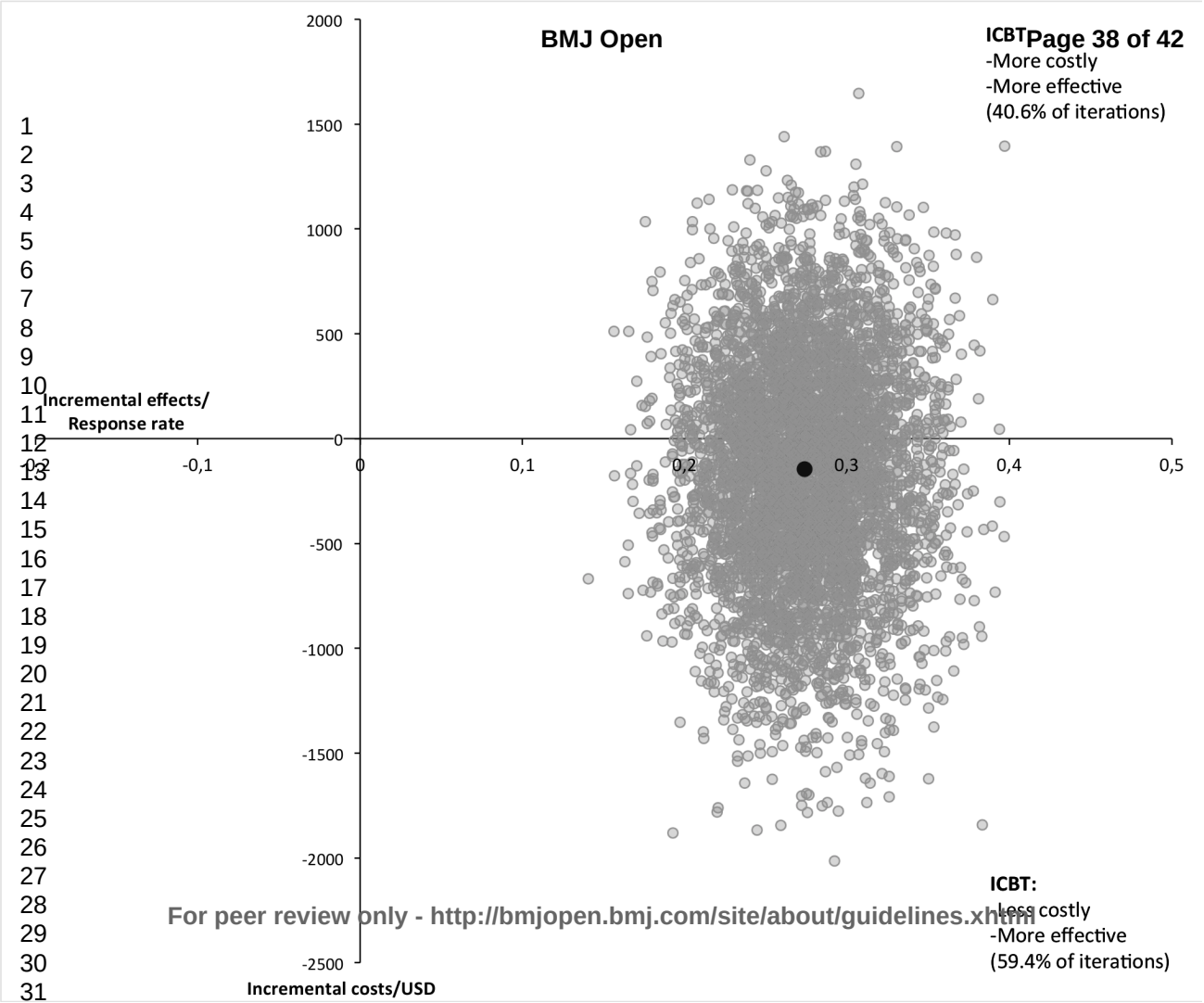
Supplementary table S1: Unit costs and sources

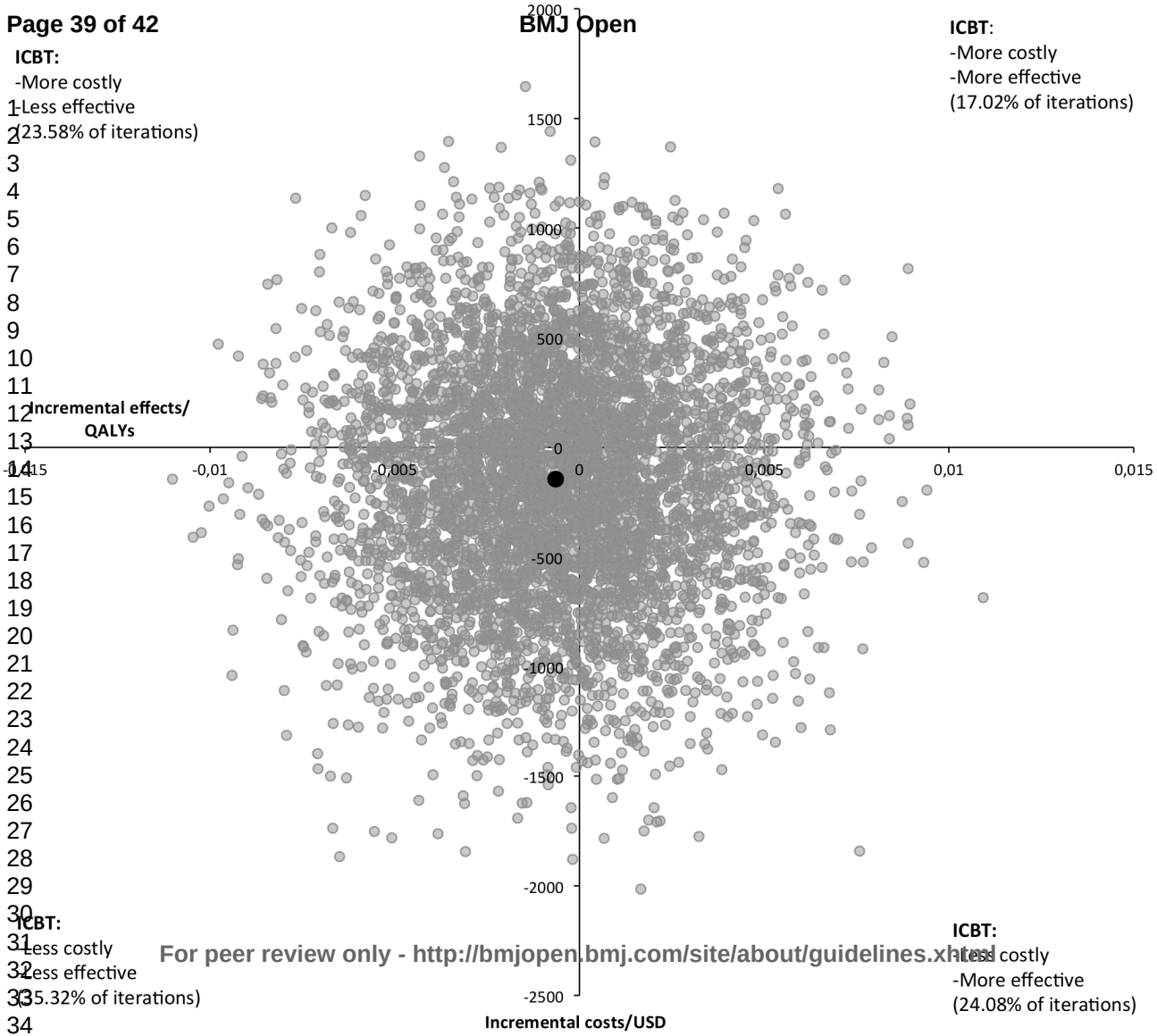
Item	Unit Cost (USD)	Source
Healthcare use (per visit)		
General practitioner (GP)	219.24	Sweden's Municipalities and Counties
Nurse	73.08	Sweden's Municipalities and Counties
Social worker	73.08	Sweden's Municipalities and Counties
Physiotherapist	73.08	Sweden's Municipalities and Counties
Specialist practitoner	385.13	Sweden's Municipalities and Counties
Chiroprator or osteopath	73.08	Sweden's Municipalities and Counties
Psychologist	73.08	Stockholm's County
Alternative medicine e.g acupuncture	73.08	Sweden's Municipalities and Counties
Medicines (Pharmaceuticals)		
Medication e.g anti-depressants	Individual product prices	Medical products agency of Sweden
Supportive resources		
Tutoring help (1 hour)	53.06	Sweden's Municipalities and Counties
Productivity loss		
Average salary/wage/hour in Sweden (2015)	31.31	Statistics Sweden
Cost of leisure time/hour	10.96	Johannesson et al. 1990
Cost/child/day for basic education	66.85	Swedish National Agency for Education
Intervention cost		
Maintenance cost (per patient)	65.08	Own estimate
ICBT clinician cost (per hour)	25.98	Average hourly psychologist wage, Statistics Sweden

Supplementary table S2: Resource use at pre- and post-intervention

Pre-intervention resource use		ICBT		Waitlist	
		mean	**sd**	**mean**	**sd**
Health care	Medical doctor visits	0,83	0,99	0,59	0,95
	Nurse visits	0,47	0,90	0,16	0,37
	Social worker visits	0,03	0,18	0,28	0,81
	Physiotherapist visits	0,20	0,81	0,31	0,78
	Specialist practitioner visits	0,33	0,84	0,28	0,58
	Chiropractor and osteopath visits	0,17	0,38	0,41	1,13
	Alternative medicine visits	0,00	0,00	0,00	0,00
	Psychologist visits	0,97	1,54	0,41	0,67
Supportive resources	Private tutoring (hours)	0,87	2,86	0,34	1,04
	Help from family and friends (hours)	5,33	14,10	6,13	16,57
Medicines	Medicine used (units)	21,87	23,36	17,63	17,82
Prescription-free medicines & supplements	Supplements used (units)	9,57	17,29	11,34	18,49
School absence	Days absence from school	1,30	1,86	1,16	1,59
	Home tutoring (hours)	0,00	0,00	0,00	0,00
Academic production loss	Days in school when feeling ill	1,50	3,25	2,38	5,87
	Production loss (0 – 10)	1,90	2,96	2,56	3,89

Post-intervention resource use		ICBT		Waitlist	
		mean	**sd**	**mean**	**sd**
Health care	Medical doctor visits	0,77	0,77	0,50	0,98
	Nurse visits	0,13	0,35	0,38	0,66
	Social worker visits	0,17	0,53	0,13	0,49
	Physiotherapist visits	0,13	0,51	0,25	0,72
	Specialist practitioner visits	0,23	0,50	0,38	0,79
	Chiropractor and osteopath visits	0,23	0,63	0,25	0,57
	Alternative medicine visits	0,07	0,25	0,00	0,00
	Psychologist visits	0,83	1,39	0,50	1,30
Supportive resources	Private tutoring (hours)	0,07	0,37	0,00	0,00
	Help from family and friends (hours)	0,50	1,58	0,81	3,29
Medicines	Medicine used (units)	15,03	17,88	10,84	13,87
Prescription-free medicines & supplements	Supplements used (units)	5,13	12,99	8,00	14,20
School absence	Days absence from school	1,75	2,76	1,47	3,65
	Home tutoring (hours)	0,20	0,81	0,13	0,71
Academic production loss	Days in school when feeling ill	2,08	4,28	2,66	5,91
	Production loss (0 – 10)	1,70	3,00	1,69	2,62





CHEERS Checklist

Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	Title page
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	p 4 - 6
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	p 8
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	p 10 - 12
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	p 10 - 12
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	p 9
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	p 6
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	n.a.
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	p 11- 12
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	p 6 - 7

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	n.a.
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n.a.
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	p 10 - 11
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	n.a.
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	p 10
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	n.a.
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	n.a.
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	p 12 - 14
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	p 14 - 17
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	p 16 - 17, p 18
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	p 19

		of methodological assumptions (such as discount rate, study perspective).	
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	n.a.
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	n.a.
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	p 19 - 22
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	p 22
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	p 23

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.